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PHOSPHATURIA.

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Phosphaturia is one of the most widely observed of all clinical phenomena. It comes before the notice of the medical profession not only as a symptom, but also as a sign. The patient complains that he is passing dirty urine or sediment in his urine and also in very many specimens the clinician will obtain a thick precipitate of earthy phosphates by heating the urine which in the cold appears perfectly clear. In either event the patient is usually said to be suffering from phosphaturia.

The literature of the subject is rather strange, for although an immense amount of work has been done in some branches, others have been almost completely neglected. For instance, there is an amazing series of original papers dealing with the quantitative estimation of phosphates, which began with Sutton in 1860 and was carried on by Bell, Doisy, Briggs, Fiske, Subarrow, Benedict, Theis and many others up to the present day. Literature dealing with the metabolism of phosphorus is also extensive and the phosphorus content of the blood under physiological and pathological conditions has received much attention.

It is when a search is made for articles dealing with urinary phosphates, their incidence in health and in disease, phosphaturia (loose term though it is) and the causes underlying phosphaturia that the literature becomes unsatisfactory. A few articles have appeared in the last decade, but these are incomplete and treat the subject very superficially. In reviewing the literature for this thesis no comprehensive article on the subject could be traced, either published as a monograph or included in a textbook. In Osler's "Modern Medicine" the subject is given a bare page. Young in his "Practice of Urology" publishes nothing under the heading of phosphaturia, although a certain amount may be gleaned on a careful search through the chapters on urinary infections and infestations and urinary lithiasis. Cabot ignores it and Cushny gives a few scattered paragraphs on the subject, but makes no attempt at a full discussion. The most extensive article published recently seems to be by A. Renner in the *"Handbuch der Urologie,"* edited by A. von Lichtenberg, F. Voelcker and H. Wildbolz and published by Julius Springer in 1927. Even here the story is far from complete.

In this thesis the technique of phosphorus estimation will be ignored except for a brief reference to those methods which were made use of to obtain the experimental results. It is proposed rather to attempt a complete discussion of the whole subject and to include the results of certain original investigations, which may throw light on points which have been hitherto ill-understood.

The thesis will be divided under two main headings: Phosphaturia in general and infected phosphaturia.

This division seems to be an uncommon one, but on so many occasions has the question of infected phosphaturia been dismissed from the literature either through motives arising from a lack of interest or a lack of knowledge, that it was determined to attempt a more extensive discussion of this portion of the subject than of any other. In textbooks and monographs infected phosphaturia is usually dismissed in some sentence such as the following: ". . . we do not include those cases of cystitis with alkaline urine, which comprise a great part of the older literature," or "phosphaturia due to infections of the urinary tract is not true phosphaturia and may be dismissed."

Infected phosphaturia cannot be dismissed in this arbitrary fashion; infection is certainly the commonest cause of permanent phosphaturia and its effects upon the organism are manifold. There are few commoner syndromes than that of chronic prostatitis—phosphaturia—neurasthenia; in addition the influence of infected phosphaturia in secondary stone building is widely recognized.

It seems, therefore that phosphaturia is made today a convenient label for a wide variety of clinical phenomena. In this respect it is comparable with such ill-defined diseases as the common cold or influenza. Like these it is not in itself dangerous to life, but an improper appreciation of its cause and an indifference to its treatment may be followed by serious and far-reaching effects.

Phosphaturia in General.

Definition and Discussion.

Phosphaturia is a term which has developed a wide and indefinite meaning. Herbert French[1] differentiates four very different types of phenomena, the presence of any one of which is usually termed phosphaturia without any clear understanding of its exact nature.

(i) Circumstances in which a greater quantity of phosphates is habitually passed in the urine than is the average maximum in health.

(ii) The spontaneous deposition of phosphates in a urine that has stood in a specimen glass until cold.

(iii) The spontaneous deposition of phosphates in the bladder, so that the urine is thick and milk-like when it is being passed.

(iv) The deposition of phosphates as a white cloud when the urine is heated.

Of these four conditions only (i) and (iii) are pathological; (ii) and (iv) are due to the external influences of heat, cold and some other factor upsetting the equilibrium which existed between the more soluble and the less soluble phosphates. The total quantity and the relative proportions of the phosphates lie within the limits of normality and these conditions are only important inasmuch as they reproduce in the test tube the apparently spontaneous precipitation of phosphates which occurs within the bladder under the conditions defined in (iii).

The condition (i) is rare, sometimes known as "phosphatic diabetes" or "essential phosphaturia." It was described by Teissier, of Lyons, in 1876 and is characterized by thirst, emaciation, aching in the loins and back and polyuria without sugar, but with an absolute excess of phosphates in the urine. Barker studied the metabolism in such a case and found it normal for carbohydrates, but the organic phosphorus percentage was high; the chief abnormality was an abnormally large amount of organic acids, so that chemically the condition was suggestive of acidosis.

The condition (iii) is of most importance, not only for its immediate and late results when it is permanent, but also because it is one of the most common urinary phenomena. It is this variety which comes within the scope of this thesis, and it is proposed to deal with many of its aspects. It should be mentioned here that unless otherwise indicated the term phosphaturia in this thesis will be strictly confined to the definition (iii), that is, the spontaneous deposition of phosphates in the bladder so that the urine is thick and milk-like when it is being passed.

Chemistry.

Phosphorus occurs in the urine in two forms, the organic compounds of phosphorus which are beyond the scope of this discussion, and the inorganic compounds. The inorganic compounds consist of the orthophosphates of various metals. These metals form two groups, sodium and potassium fall in one group and calcium and magnesium into the other group. The phosphates of sodium and potassium are known as the alkaline phosphates and the phosphates of calcium and magnesium as the earthly phosphates.[1] The phosphoric acid radicle is trivalent and forms three classes of salts. Every valency may be satisfied by a metal or two by a metal and one by a hydrogen atom or one by a metal and two by hydrogen atoms. These salts may be written as follows:

NaH_2PO_4 ..	Monosodium phosphate
Na_2HPO_4 ..	Disodium phosphate
Na_3PO_4	Trisodium phosphate
$CaH_4(PO_4)_2$ ..	Monocalcium phosphate
$CaHPO_4$ ..	Dicalcium phosphate
$Ca_3(PO_4)_2$ ..	Tricalcium phosphate

Monosodium phosphate and disodium phosphate are very readily soluble in water and are never precipitated under any physiological or pathological condition. It is on the relative proportion of these two salts that the reaction of the urine depends. The monosodium phosphate is distinctly acid, solutions having a pH of 4·82; the disodium phosphate is slightly basic and has a pH of 7·45. The trisodium phosphate is only formed by the action of very strong alkali on phosphoric acid and cannot be said to exist in urine.

The calcium and magnesium phosphates occur in smaller quantities in the urine than the phosphates of soda and potash and are far less soluble. The ratio of earthy phosphates to alkaline phosphates in the urine is said to be about 1:4 on the average. This finding does not agree with the experimental results recorded below, in which the ratio is approximately 1:2. However, the conditions under which these figures were obtained were not the same. The monocalcium phosphate is the most soluble, dicalcium phosphate being far less soluble and tricalcium phosphate is practically insoluble. Like the trisodium phosphate, tricalcium phosphate probably does not enter into the present discussion.

It is seen that if any change takes place in the solution which tends to favour the formation of the less soluble dicalcium phosphate, all excess of dicalcium phosphate over and above its saturation point will be precipitated. This may be accomplished in several ways.

1. The amount of disodium or dipotassium phosphate may increase and the following reaction take place:

$$Na_2HPO_4 + CaH_4(PO_4)_2 = CaHPO_4 + 2NaH_2PO_4$$

The dicalcium phosphate being almost insoluble will be precipitated.

2. If the urine is heated, the dicalcium phosphate is decomposed into monocalcium phosphate and tricalcium phosphate thus:

$$4CaHPO_4 = Ca_3(PO_4)_2 + CaH_4(PO_4)_2$$

If after boiling the solution is allowed to stand, it tends to return to its original condition, the precipitated tricalcium phosphate being redissolved; this occurs quickly if in place of boiling, the solution is merely heated sufficiently to produce the decomposition.[2]

3. If the urine is made alkaline through any cause other than an excess of disodium phosphate, the earthy phosphates will again be precipitated. Experimentally this is done in the test tube by the addition of ammonia or in the bladder by the ammonia formation of urea-splitting bacteria. Here the ammonia forms calcium and magnesium ammonium phosphates which are also insoluble, and a precipitate comes down.

In short, the inorganic phosphates of the urine exist as salts of sodium and potassium and calcium and magnesium. In the presence of alkalis the calcium and magnesium salts are precipitated.

Physiology.

Temporary Phosphaturia.

Phosphates are always present in the urine and vary not only in type, as has been seen before, but also in quantity from hour to hour. On the average two to two and a half grammes of phosphorus pentoxide are excreted in the urine in twenty-four hours. It has also been seen that with a suitably low hydrogen ion concentration the earthy phos-

[1] This nomenclature is convenient but confusing. The term alkaline does not imply that the phosphates are alkaline in reaction, but that they are phosphates of that group of metals known as the alkaline metals, sodium and potassium being the most commonly occurring members of this group. Earthy phosphates are the phosphates of the alkaline earths of which calcium and magnesium are the most widely distributed.

phates will be precipitated. It should be remembered that the conventional pH figures are logarithms and pH 7·0 means that the solution is a 10^{-7} normal solution of hydrogen ions. Therefore, as the exponent becomes 6, 5, 4 and so forth, the number of hydrogen ions increases and pH 4·5 is greater than pH 9·0. The question of a high or low phosphate content is not very material. Indeed it will be shown in the experimental results that phosphaturia occurs more often when the total phosphate content is below the average. Also, a phosphaturiac may on one occasion void urine which is faintly milky, and on another a specimen which has almost the consistency of tooth paste.

Now the hydrogen ion concentration of the urine is almost completely determined by the type of phosphates which it contains. Henderson and Palmer[3] and later Cushny[4] have shown that by the administration of monosodium phosphate and of sodium bicarbonate the highest pH value obtained was 4·70 and the lowest was 8·70. Henderson and Palmer also showed that the variation in the reaction of the urine lies between the limits of acidity of monosodium phosphate and of alkalinity of disodium phosphate; that is, between pH 4·82 and pH 7·45, with a mean value of pH 6·00.[5] Howe and Hawke confirmed this when they showed that under fasting conditions the urinary pH was as high as 5·63 and later on fell to 9·00 after the fast was broken.[6]

If the question of infection is neglected, the ultimate cause of the continually varying hydrogen ion concentration of the urine (as opposed to the proximal cause, discussed under the heading of chemistry) is found in the following facts. The necessity for the body fluids to remain constant in reaction for the maintenance of life renders it important that there shall be organs which can deal with excess acidity or alkalinity in these fluids. These organs are the lungs and the kidneys. The lungs deal with all volatile constituents and the kidneys with the non-volatile constituents.

The wide range of foods ingested by the human organism is governed by no close limits of reaction and the blood will frequently be flooded with absorbed products of digestion which at one time will be more acid and at another time more alkaline than the blood. Owing to the presence of buffer salts the reaction of the blood remains very constant under all conditions, but nevertheless it may contain an excess of acid or basic ions. Thus, according as to whether there is an excess of acid or of alkali, so will the urine have a higher or lower hydrogen ion concentration. In general there is a smaller intake of basic radicles in the food than of acid radicles, hence the reaction of the urine is more often acid than alkaline.

There are certain other physiological and pathological conditions besides food intake which react on the hydrogen ion concentration of the urine. The so-called alkaline tide which occurs after meals, depends on the large quantity of hydrochloric acid secreted in the stomach for digestion.[7] This drain on the acid ions leaves a preponderance of basic ions in the blood and an equivalent amount of alkali is rapidly excreted in the urine mainly in the form of disodium phosphate. The physiological acidosis of starvation and the pathological acidosis of *diabetes mellitus* are associated with very acid urine. This represents an attempt on the part of the body to rid itself through the kidneys of the normal or abnormal acid products of metabolism. Morse[8] states that the reaction of the urine runs parallel with the diet, an average vegetarian diet giving pH 6·6, whereas a high protein diet gives pH 5·9. Starvation, which involves an almost exclusive protein metabolism, produces a urine of maximal acidity, pH 5·0.

The urine may also become temporarily alkaline as the result of ingesting alkaline carbonates or certain salts of tartaric or citric acid which may be transformed into carbonates within the organism. Ingestion of acid fruits, oranges, lemons, peaches and the like causes the formation of an alkaline urine. This is due to the fact that the ash of such fruit is alkaline and when the fruit is metabolized in the body, carbonates are formed. On the other hand bread and cereals yield an acid ash and an acid urine. Here follows a list compiled by Sherman and Gettler[9] showing the main acid forming and base forming articles of diet.

TABLE I.

Article of Food	Excess Acid or Base in terms of Normal Solutions, Cubic Centimetres per 100 Grammes	
	Acid	Base.
Apples	—	3·76
Asparagus	—	0·81
Bananas	—	5·56
Beans (dried)	—	23·87
Beans (lima, dried)	—	41·65
Beets	—	10·86
Cabbage	—	4·34
Cantaloup	—	7·47
Carrots	—	10·82
Cauliflower	—	5·33
Celery	—	7·78
Crackers	7·81	—
Eggs	11·10	—
Egg white	5·24	—
Egg yolk	26·69	—
Fish (haddock)	16·07	—
Lemons	—	5·45
Lettuce	—	7·37
Meat (lean beef)	13·91	—
Milk (cow's)	—	2·37
Oatmeal	12·93	—
Oranges	—	5·61
Potatoes	—	7·19
Prunes	—	24·40
Raisins	—	23·68
Rice	8·10	—
Wheat (entire)	9·66	—

Plums, prunes and cranberries yield an alkaline ash, but serve to increase the hydrogen ion concentration of the urine because of their benzoic acid content, this acid being synthesized with glycocoll in the kidney and elsewhere to form hippuric acid.

From what has been stated in the preceding paragraphs it can be seen that there are ever present a multitude of causes, all within the probabilities of normal daily life, which are constantly altering the

amount and type of phosphates present in the urine and therefore the reaction. Very often the reaction becomes sufficiently alkaline to precipitate the earthy phosphates and this precipitation may occur either before or after voiding. If it occurs before voiding, the patient will pass milky urine and the diagnosis of phosphaturia will be made. It must be insisted on again, however, that the presence of phosphaturia need not depend on the amount of earthy phosphates excreted; it is the reaction of the urine, depending on the type of phosphates excreted which determines the presence or absence of phosphaturia, together with another factor which will now be discussed.

It is unlikely but not impossible that earthy phosphates can be secreted through the renal tubules in the precipitated condition.[1] Yet, on many occasions earthy phosphates are precipitated in the renal pelvis, on other occasions in the bladder and on others not until the urine has been voided. The question arises as to what it is that keeps these salts in solution for a greater or less period of time when the reaction of the urine is alkaline. It is well known that if a urine be analysed and an attempt made to dissolve the constituents in water, it will be found that they will not dissolve completely. The urine seems, therefore, to be in a somewhat similar condition to a supersaturated solution and different investigators have named this or that protein as being responsible for keeping the superabundance of solid in solution. Little is known about the mechanism at present, but certain external influences seem to remove this protective colloid property and allow the solids to be precipitated. Investigators today seem to regard this phenomenon as being closely bound up with surface tension. Thus Young points out that any foreign body in the bladder which lowers the surface tension, will be rapidly encrusted with phosphates.[10] Pure paraffin does not lower the surface tension and remains for long periods free from phosphates. Renner, too,[11] coordinates the familiar phosphate pellicle in urine with the same surface tension effect. Needless to say the importance of this factor in stone formation cannot be overestimated.

Beer[12] has made some interesting observations on this question. He suggests that phosphaturia is a peripheral and local phenomenon and it is not due to any particular metabolic disturbance. He quotes certain cases.

In one patient both ureters were catheterized during cystoscopy. Clear urine came from the right kidney and milky urine from the left. He claims that this was an instance of unilateral phosphaturia and was due to the passage of the catheter up the ureter. This was probably true, but it must be remembered that one kidney may have had an impaired function with regard to phosphates and was retaining sufficient monosodium phosphate to lower to a material degree the hydrogen ion concentration of the urine from that side. Morse[13] says that in chronic nephritis there is retention of phosphates in the blood, which causes a lower total acid reaction through the kidneys and a tendency towards alkaline reaction or an actual alkalinity of the urine.

His second patient was a man who voided milky urine containing phosphates and also carbonates. Immediate catheterization of the bladder drew off several ounces of clear, brilliant, normal urine. He says that it is evident in this observation that the bulk of the urine was changed in its passage through the male urethra and that the process must have been a local one, as the residue obtained within a few minutes was clear and brilliant. It would have been interesting and confirmatory if the earthy and alkaline phosphate content of both specimens had been estimated. Unfortunately this does not appear to have been done.

The third case is similar to the second; here it was a woman who voided milky urine and afterwards the catheter drew off thirty cubic centimetres (one ounce) of clear brilliant urine. He concludes by saying that it seems that we must conclude that there is a phosphaturia due to local urinary tract conditions in which urinary infections do not play a part.

Several cases of this type have been noticed at the Royal Prince Alfred Hospital. In two of them quantitative phosphate determinations were made. In one instance the ureteral specimens were clear and the bladder specimen milky. Analysis showed that all three specimens had the same phosphate content; for example the total phosphate was equivalent to forty milligrammes of phosphorus pentoxide per hundred cubic centimetres, the alkaline phosphate was equivalent to thirty milligrammes per hundred cubic centimetres and the earthy phosphates were equivalent to ten milligrammes per hundred cubic centimetres.

In the other instance the bladder specimen was clear and both ureteral specimens milky. Here the total phosphate content of all three was sixty milligrammes of phosphorus pentoxide per hundred cubic centimetres, the alkaline phosphates were thirty-five milligrammes per one hundred cubic centimetres and the earthy phosphates were twenty-five milligrammes per hundred cubic centimetres.

Calculating the percentage of earthy phosphate in the total showed in one that it was 33% and in the other that it was 41·7%. If the phosphate estimation tables given below are consulted, it will be seen that phosphaturia with these percentages of earthy phosphates is common.

These results go to strengthen Beer's assertions and indeed, if the hypothesis is granted that alkaline urine is secreted by the kidney with all the phosphates in solution, the conclusion that some local influence determines phosphaturia becomes inevitable.

From the foregoing discussion it is seen that temporary phosphaturia is a not infrequent happen-

[1] Cushny points out that the carmine injection experiments of Heidenhain and others repeatedly show a diffusely stained tubular epithelium and granular dye in the lumen. It is common to observe in necropsy specimens from patients with chronic nephritis, the presence of deposits of calcium salts in the cortex.

ing which is due to two factors, one, the constantly changing nature of the human dietetic environment and the other, the local causes which remove or lessen the protective colloid function of the urine. The main features of this type of phosphaturia are its sporadicity and its evanescence. In these days the human dietary is so wide and human tastes are so varied that it is seldom that a dietetic phosphaturia will occur on two consecutive occasions. It is the least harmful of any type of phosphaturia and its occasional presence should be regarded as a sign of normality rather than a pathological manifestation.

Permanent Non-infected Phosphaturia.

Permanent phosphaturia may be best treated in two sub-classes, non-infected permanent phosphaturia and infected permanent phosphaturia. In this section it is proposed to deal with non-infected permanent phosphaturia only, as the experimental work done on the infected variety makes it too large a subject to deal with under a subheading.

Non-infected permanent phosphaturia is defined by Renner[11] by a process of exclusion. He says:

> All cases in which the urine is alkaline from a definite cause and in which as a consequence a precipitate comes down, are not reckoned as phosphaturia In addition we do not include those cases of cystitis with alkaline urine which comprise a great part of the older literature. Neither do we include those cases where the urine becomes alkaline through vegetables or those foods particularly rich in bases; even less do we consider here the appearance of a sediment after meals or after vomiting strongly acid material (Quincke). The secretion of an alkaline urine through hyperacidity must also be excluded before one can diagnose a true phosphaturia.

According to the literature permanent non-infected phosphaturia seems to be due to two main causes, neurasthenia and some inability of the bowel to excrete earthy phosphates.

With regard to the phosphaturia of neurasthenic origin, a very important point arises. It is notorious that among the most introspective and neurasthenic of all classes of patients are those who suffer from chronic urinary disease and above all those who suffer from chronic prostatitis. Permanent phosphaturia is so often associated with chronic prostatitis and also with neurasthenia that the three seem to form a definite syndrome.

The experimental results include several cases of prostatitis, neurasthenia and phosphaturia; in all the urine or prostatic smears contained organisms capable of culture and the organism cultivated in all split urea and produced ammoniacal urine. Moreover, and this is the important observation, in no case in this series were the earthy phosphates in greater absolute quantities than normal. The total phosphates were within normal limits and the alkaline and earthy phosphates bore a normal relation one to the other.

Therefore there seem to be at least some neurasthenics with phosphaturia who are really suffering from infected phosphaturia and in these patients there is no real increase of earthy phosphates at all. No neurasthenic suffering from phosphaturia should be regarded as having an uninfected urinary tract except after a most rigorous search for organisms; a neurasthenic with true non-infected phosphaturia is almost certain to have an absolute increase in his earthy phosphate excretion.

Considerable attention has been paid to non-infected permanent phosphaturia in literature. Probably the best *résumé* of the subject is by Renner,[11] but even he does not accentuate the crucial points of excluding infection and of differentiating between an absolute increase of earthy phosphates and a urine with normal phosphate content which has been artificially alkalinized. He points out that for precipitation of earthy phosphates to occur, the phosphorus pentoxide-calcium oxide ratio must be below normal; the range of normality lies between 7 and 42. If the phosphoric acid excretion diminishes or the alkali excretion increases, that is the quotient is small, more secondary alkaline phosphates are produced and the amount of primary phosphates is diminished. He quotes Sindter who asserted that clear urine could exist with a quotient of below 7, while Umber observed a patient who excreted cloudy urine with a quotient of 29. These apparent anomalies may be explained if the previously mentioned protective colloid is taken into consideration. Some unknown factor reinforcing or inhibiting the action of this colloid would either cause a clear urine with a low quotient or a milky urine with a high quotient. However, this is speculation and much work remains to be done on this portion of the subject.

Renner appears to agree with those investigators who assert that non-infected permanent phosphaturia is due to an absolute increase in the urinary calcium which has been brought about by a partial or complete inability on the part of the bowel to excrete its share of the body's calcium. Absolute proof, as he says, is lacking for this, but the work of Domarus and Tobler who made quantitative experiments on the total intake and output of calcium both by the bowel and by the urine, is very strongly in favour of its truth.

Renner also points out that the absolute amount of phosphate has no influence on precipitation, but says that it is due to a variation in proportion. This must not be misunderstood. It was pointed out above that for the production of temporary phosphaturia, the proportion was all that mattered; but in permanent phosphaturia some constant factor must be introduced and this must be one of only three. Either there is a constant decrease in the alkaline phosphates, a constant stant increase in the earthy phosphates or an inhibition of the protective colloid. Apart from experimental diets there is no way in which the alkaline phosphates can be decreased over a long period of time and we know little on the subject of the protective colloid; but much evidence has been brought forward that in certain intestinal conditions the absolute amount of earthy phosphates may be permanently increased. Sotbeer,[14] for example, reports a case of phosphaturia with in-

testinal disturbance in which the urine contained nearly four times as much lime as in health. His explanation is that the large intestine, the natural secretory organ for lime salts, was unable by reason of disease to excrete the lime. Hence its passage through the kidneys.

To sum up, permanent non-infected phosphaturia seems to be due either to neurasthenia or to intestinal derangements. Up to the present, the reason why neurasthenia causes phosphaturia remains obscure and it is a far more common experience in urological practice to find that phosphaturia causes neurasthenia. Many questions remain to be elucidated, but the weight of evidence seems to show that permanent phosphaturia is caused by an absolute increase in the earthy phosphates excreted by the urine and that this is secondary to an inability on the part of the large bowel to excrete its proper amount of earthy phosphates.

Experimental Work.

One hundred and eighty-eight specimens of urine were quantitatively examined for their phosphate content. The uranium method of Sutton[15] with potassium ferrocyanide as the indicator was used throughout. Results by this method are said to lie slightly high and this was checked by performing a series of estimations by the colorimetric method of Benedict and Theis.[16] This seemed to indicate that the results as obtained by the uranium method were about 10% too high. In the tables given below, this error has not been allowed for, as the conclusions have been arrived at almost entirely from a consideration of the relative phosphate values rather than the absolute values; however, this error should be kept in mind when the figures are examined.

In this investigation the estimation of twenty-four hour samples of urine was definitely contraindicated. A twenty-four hour sample can give information only as to the total phosphates excreted over a period of time which is far too long. Temporary phosphaturia, as has already been pointed out, is so evanescent that it usually occurs only at a single act of voiding during the day. A mixed sample taken over twenty-four hours is always acid except in infected cases and shows no deposition of phosphates. In addition, it is by the examination of only a single specimen that any idea can be obtained of the upper and lower limits of phosphate excretion. The twenty-four hour sample will always give an average figure in this regard.

Out of 188 specimens examined 33 were alkaline and all but two of these showed a precipitate of earthy phosphates. This represents a percentage of 17·5 of the total specimens.

The maximum amount of total phosphates found in any specimen was 450 milligrammes of phosphorus pentoxide per hundred cubic centimetres. The lowest was fifteen milligrammes per hundred cubic centimetres. The maximum amount of alkaline phosphates found in any specimen was 370 milligrammes of phosphorus pentoxide per hundred cubic centimetres and the lowest was zero. The maximum amount of earthy phosphate found in any specimen was 130 milligrammes of phosphorus pentoxide per hundred cubic centimetres and the lowest was zero. For all cases the average total phosphate was 129 milligrammes of phosphorus pentoxide per hundred cubic centimetres which gives a figure of 1·93 grammes in a twenty-four hour sample of one and a half litres. This is of interest, as it shows a fair correspondence with the twenty-four hour phosphate excretion as given by various investigators. Results are usually given as lying between two and two and a half grammes of phosphorus pentoxide *per diem*. The figure is low because there were far more day specimens examined than night specimens and it will be seen later that the specimens passed at bedtime and on rising are particularly rich in phosphates.

In all cases the average amount of alkaline phosphate was 88 milligrammes of phosphorus pentoxide per hundred cubic centimetres and of earthy phosphates, 39 milligrammes of phosphorus pentoxide per hundred cubic centimetres. This gives a ratio of alkaline to earthy phosphates of slightly more than 2: 1 and a percentage of earthy phosphates to total phosphates of 31%. The ratio between alkaline and earthy phosphates is usually quoted as 4:1, but this figure was almost certainly obtained by the analysis of twenty-four hour specimens.

The average total phosphate content of the urine of the thirty-three persons with phosphaturia was 87 milligrammes of phosphorus pentoxide per hundred cubic centimetres; the average alkaline phosphate was 48 milligrammes of phosphorus pentoxide per hundred cubic centimetres and the average earthy phosphate was 38 milligrammes of phosphorus pentoxide per hundred cubic centimetres. The percentage of earthy phosphate to total phosphate was 44·2. Comparing these figures with the normal, one point immediately becomes apparent, namely that the amount of earthy phosphates is not greater than the average of all samples. However, unless the matter is dissected still further, any conclusions drawn from this may be erroneous.

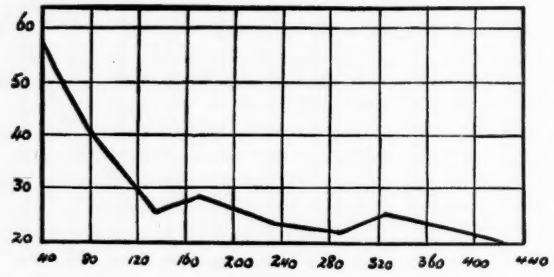
From the discussion which has gone before, it was seen that phosphaturia may be divided into three classes: temporary phosphaturia, permanent non-infected phosphaturia and permanent infected phosphaturia. It has been pointed out that infected phosphaturia is due to the deposition of phosphates by urea-splitting organisms and to no metabolic factor whatever. The quantitative phosphate estimation of these cases, therefore, should give normal results.

Before these figures are given, however, one very important point must be mentioned. It became increasingly obvious during the investigation that in order to obtain a true comparison between normal urine and milky urine, it was necessary to make use of a series of specimens of normal urines which contained approximately the same amount of total phosphates as the milky urine. A reference to Table II and Graph I should make this clear.

TABLE II.

Average Total Phosphate Content.	Average Alkaline Phosphate Content.	Average Earthy Phosphate Content.	Earthy Phosphate in Total.	Limits of Total Phosphate within which Calculation was made.	Number of Specimens
			%		
40·2	16·9	23·3	58·0	30–59	30
79·0	46·0	33·0	41·8	60–109	41
134·0	99·0	35·0	26·1	110–159	34
179·0	127·0	52·0	29·0	160–209	16
227·0	172·0	55·0	24·2	210–259	10
285·0	221·0	64·0	22·4	260–309	8
325·0	241·0	84·0	25·8	310–359	7
422·0	351·0	71·0	20·2	360–450	6

The phosphate is expressed as phosphorus pentoxide in this and the succeeding tables.



GRAPH I.
The ordinate represents percentage of earthy phosphate.
The abscissa represents milligrammes of total phosphate.

It will be noticed that for a total phosphate content of 150 milligrammes per hundred cubic centimetres and upwards, the relative amount of earthy phosphate lies very constantly between 20% and 25%. Below this figure, however, the relative amount of earthy phosphate rapidly increases. In other words, as urine becomes more dilute both earthy and alkaline phosphates diminish proportionally, but below a total phosphorus pentoxide content of about 150 milligrammes per hundred cubic centimetres the alkaline phosphates diminish in quantity far more rapidly than the earthy.

Thus the necessity will be seen of comparing concentrated urine with concentrated urine and dilute urine with dilute urine.

In Table III the average of four samples of infected phosphaturia urine is compared with normal specimens of the same total phosphate content.

TABLE III.

Phosphate.	Infected Phosphaturia.	Normal.
Total	118 mg. %	134 mg. %
Alkaline	86 mg. %	99 mg. %
Earthy	32 mg. %	35 mg. %
Earthy in Total.. ..	26·9 %	26·1 %

Table IV is compiled from nine other samples from infected patients who were being treated with internal hydrotherapy. The results were very dilute, but it will be noted that even here the proportions of alkaline and earthy phosphates are well within the range of normality.

TABLE IV.

Phosphate.	Infected Phosphaturia.	Normal.
Total	35 mg. %	40·2 mg. %
Alkaline	12·5 mg. %	16·9 mg. %
Earthy	22·5 mg. %	23·3 mg. %
Earthy in Total.. ..	64·5 %	58·0 %

Turning now to permanent non-infected phosphaturia, it has been previously asserted that this condition is due to an absolute excess of earthy phosphate in the urine. Hence the alkaline phosphates should be found unaltered and there should be simply an increase in the earthy phosphates. Table V is compiled from nine samples of urine of persons with permanent non-infected phosphaturia compared with the average phosphate content of those normal specimens which contain a similar amount of alkaline phosphate.

TABLE V.

Phosphate.	Permanent Non-Infected Phosphaturia.	Normal.
Total	108 mg. %	79 mg. %
Alkaline	48 mg. %	46 mg. %
Earthy	59 mg. %	33 mg. %
Earthy in Total.. ..	54·6 %	41·8 %

It is seen from this table that there is both an absolute increase in the earthy phosphate content as well as a relative one. The existence of phosphaturia in these circumstances cannot altogether depend on the amount of earthy phosphates in the urine. Here again the all important factors are the reaction of the urine, as determined by the alkaline phosphates and also the protective colloid. However, if Renner's statement be accepted,[11] that an increase in the calcium oxide content of the urine causes a formation of the disodium and potassium phosphates at the expense of the monosodium and potassium salts, then on the average permanent phosphaturia will be caused by an increase in the earthy phosphates. There are doubtless several patients in the series in whom earthy phosphates are permanently increased and there is no deposition of phosphates. This could be caused by a strong protective colloid function in the urine. These conditions will remain undiagnosed as permanent phosphaturia unless a quantitative estimation of many specimens or of twenty-four hour specimens is made. However, permanent phosphaturia of this type has little clinical bearing as the urine is secreted in a clear condition, but the probable existence of these cases of concealed permanent phosphaturia must be taken into consideration in any work that is done on the subject.

Lastly there is temporary phosphaturia in which two factors are concerned. The one is the constantly changing quantity and quality of the phosphate output due to the need to maintain the reaction of the

blood and the other is the protective colloid of the urine. If the protective colloid were not present, as soon as the reaction of the urine reached a certain value, the earthy phosphates would be precipitated. However, the protective colloid appears to be very variable in its action, as two specimens in this series were definitely alkaline and contained no phosphate precipitate, although there were considerable amounts present, thirty milligrames in each hundred cubic centimetres in one and forty milligrammes in each hundred cubic centimetres in the other. Unfortunately the hydrogen ion concentration of these specimens was not determined.

Another point of interest is that occasionally very high percentages of earthy phosphates were recorded in acid and clear urine. The highest observed was 93% of earthy phosphate in clear urine and there were many specimens which contained 80% and over. As against this, one specimen of milky urine contained only 19% of earthy phosphates and there were several readings of under 30%; the average for all specimens being 31%. It seems, therefore, that the relative amounts of alkaline and earthy phosphates have little effect upon the presence or absence of temporary phosphaturia, but rather it depends on the quality of the phosphates present, that is, whether they are mono- or diphosphates and also upon the protective colloid. In Table VI the condition in eleven cases of temporary phosphaturia is contrasted with the normal.

TABLE VI.

Phosphates.	Temporary Phosphaturia.	Normal.
Total	101 mg. %	104 mg. %
Alkaline	64 mg. %	70 mg. %
Earthy	37 mg. %	34 mg. %
Earthy in Total.. ..	37 %	32·7 %

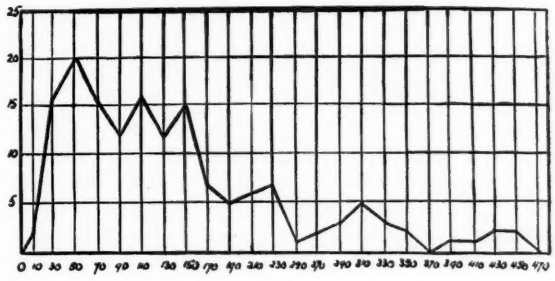
It will be seen that the results are almost identical. Thus the conclusion may be drawn that temporary phosphaturia occurs with low as well as with high relative earthy phosphate content and also that the earthy phosphate is not absolutely increased.

With regard to the diurnal fluctuation in the amount of phosphate present in the urine, Table VII gives the results of thirty phosphate estimations on the same individual, of which fifteen were taken between the hours of 9 a.m. and 9 p.m. and fifteen between the hours of 9 p.m. and 9 a.m. Apart from the great increase in the total phosphates in the night urine, the most interesting point to be noticed is the very slight increase in the earthy phosphates. Almost the entire increase is due to the alkaline phosphates.

TABLE VII.

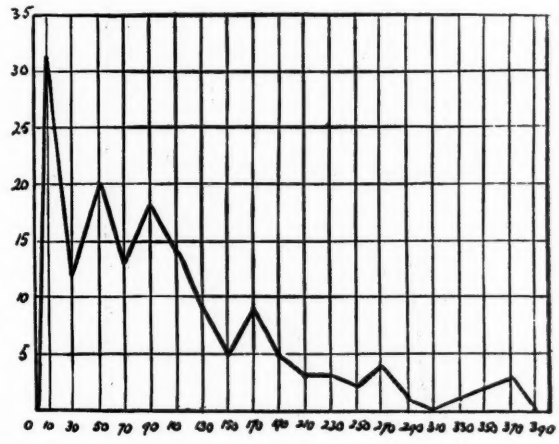
Phosphates.	9 p.m. to 9 a.m.	9 a.m. to 9 p.m.
Total	331 mg. %	93 mg. %
Alkaline	272 mg. %	53 mg. %
Earthy	59 mg. %	40 mg. %
Earthy in Total.. ..	17·8 %	43 %

Finally, four graphs are presented demonstrating the variation in the total phosphates, the alkaline phosphates, the earthy phosphates and the percentage of earthy phosphates in the total. These need no comment save that the constancy of the earthy phosphates is remarkable.



GRAPH II.

The ordinate represents number of specimens examined. The abscissa represents milligrammes of total phosphate.



GRAPH III.

The ordinate represents number of specimens examined. The abscissa represents milligrammes of alkaline phosphates.

Conclusions.

1. The term phosphaturia is too loosely used and should be restricted to one type of phenomenon.
2. The most important type of phosphaturia is the voiding of milky urine.
3. There are two types of phosphates in the urine, alkaline phosphates and earthy phosphates.
4. The reaction of the urine depends on the nature of the alkaline phosphates present in it.
5. When the urine becomes sufficiently alkaline, the earthy phosphates are precipitated.
6. Temporary phosphaturia is caused by a number of metabolic factors, the constant feature of which is an increase in the total akali of the body fluids. The kidneys excrete the excess of alkali and the earthy phosphates are precipitated in the urine.
7. The presence of protective colloid in the urine may prevent the deposition of phosphates.

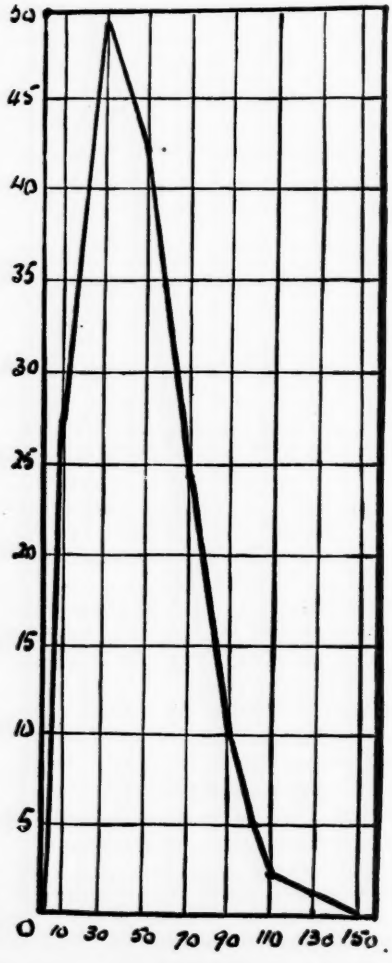
8. Permanent phosphaturia may be divided into permanent non-infected phosphaturia and permanent infected phosphaturia.

9. Permanent non-infected phosphaturia is said to be due to two causes, neurasthenia and the inability of the large bowel to excrete its quota of earthy phosphates.

10. Many cases of neurasthenic phosphaturia are really due to local urinary tract infection and the neurasthenia is the result and not the cause of the phosphaturia.

11. In 188 specimens of urine quantitatively examined for phosphates, 33 were alkaline and of these all but two showed a precipitate of phosphates.

12. In all specimens examined the ratio of alkaline phosphates to earthy phosphates was about 2:1. The figure obtained by the analysis of twenty-four hour specimens is 4:1.



GRAPH IV.
The ordinate represents number of specimens examined. The abscissa represents milligrammes of earthy phosphate. Note the extremely narrow limits of variation.

13. In all cases of phosphaturia the amount of earthy phosphate excreted was not greater than the earthy phosphate content of the clear specimens.

14. Both the alkaline and earthy phosphate content of the urine of patients with infected phosphaturia were within normal limits.

15. The urine of permanent non-infected phosphaturia showed both an absolute and a relative increase in the earthy phosphate content.

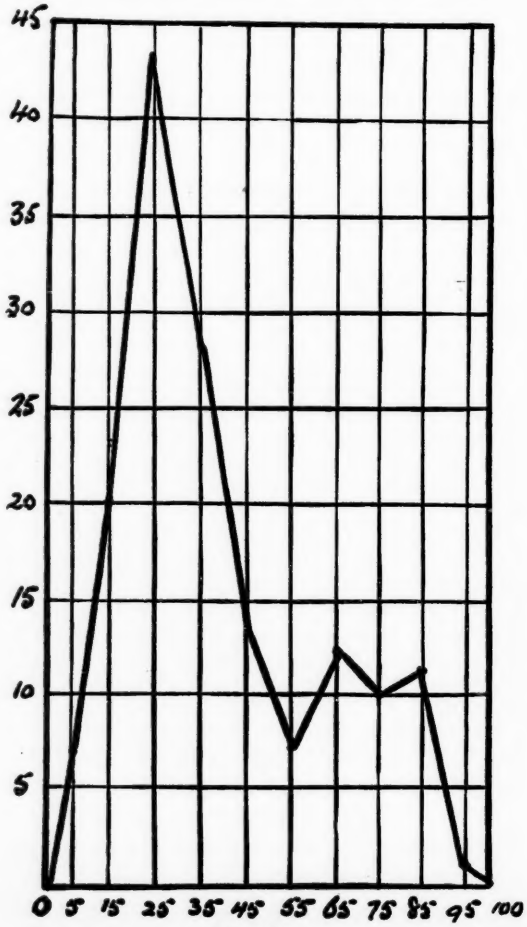
16. The urine of persons with temporary phosphaturia showed no deviation in phosphate content (quantity) from the normal.

17. The earthy phosphates are very constant in amount in urine of all concentrations.

18. As the alkaline phosphates decrease, the earthy phosphates tend to remain constant and the relative amount of earthy phosphate increases.

19. Many subjects pass larger quantities of earthy phosphates than normal, but the protective colloid in the urine prevents precipitation.

20. The night urine contains far more phosphates than the day urine.



GRAPH V.
The ordinate represents number of specimens examined. The abscissa represents percentage of earthy phosphates.

A Note on Treatment.

From the preceding analysis of phosphaturia in general it is seen that there are really three distinct conditions: temporary phosphaturia, permanent phosphaturia of non-infective origin and permanent phosphaturia of infective origin. The patient will soon tell the clinician if his trouble is temporary or permanent and if it is temporary and there is no other pathological process causing it, all that is needed is a reassurance that all is well. If, on the other hand, the trouble is permanent, certain investigations should be undertaken without delay. The genito-urinary tract should be thoroughly investigated for focal infection and if this is found to be present, the treatment should be directed towards the eradication of this focus rather than towards the phosphaturia. It will be found that attempts to clear up the phosphaturia while infection is present will end in failure. If the clinician finally convinces himself that he is dealing with a true non-infected phosphaturia, his efforts should be directed in two directions. First, he should attempt to produce a return to normal in the phosphate excretion of the bowel by attention to any constipation, colitis *et cetera* which may be present, and secondly, he may attempt to reduce the phosphaturia by giving monosodium phosphate or other urinary acidifiers by mouth and advising the patient as to his diet. In view of the findings it appears that free fluids are not indicated while the urine is alkaline, owing to the fact that the more dilute a urine becomes, the greater the relative amount of earthy phosphates and, of course, the more akaline it becomes.

Infected Phosphaturia.

Discussion.

It has already been pointed out that infected phosphaturia occupies a very small place in the literature. A certain amount of work has been done on urea-splitting organisms, but in the great majority of instances these organisms have been obtained from the soil and little is known about the parasitic bacteria which inhabit the human urinary tract. In the present investigation it was determined to carry out routine examinations of all bacteria grown from the urine of patients at the Royal Prince Alfred Hospital and elsewhere over a certain period. In all a series of two hundred consecutive cultures were obtained and the number of organisms which displayed definite urea-splitting properties exceeded all expectations. Special pains were taken to avoid duplication of results, in order to give as true a picture as possible of the number of urea-splitting organisms in the total.

The chemical mechanism by which urea is split into ammonia, is in the nature of an enzyme reaction. It is familiar to the biochemist in the estimation of the blood urea. Here the ferment used is urease and is commonly obtained from the soy or jack bean. While at present no indisputable evidence has been brought forward that the ferment concerned in bacterial urea-splitting is identical with the urease of the soy bean, yet their behaviour is very similar and the chemical reaction which they produce is identical. Jacoby[17] has brought forward evidence which would support the view that the soy bean urease differs from the bacterial urease. He found that glucose in the medium greatly accelerated the action of the bacterial urease, while the soy bean urease was only slightly influenced by the action of glucose. The chemical equation is as follows:

$$(NH_2)_2CO + 2H_2O = (NH_4)_2CO_3$$

Urea — Ammonium carbonate

The following is a brief summary of the principal work done on the subject.

Pasteur[18] apparently made the first observation that ammoniacal decomposition of the urine was bacterial in origin. Since then many investigators have studied the subject from different angles. That urea is broken up into ammonia and carbon dioxide was described by Schnitzler.[19] Brodmeier[20] investigated the influence of sugars on the fermentation process, as also did Jacoby[17][21] and later Ishikawa.[22] Laschina[23] stated that the field of a solenoid had no accelerating effect on the bacterial decomposition. Geilinger[24] reported that of seventy-two cultures of urea-splitting organisms obtained from soil and manure, four were able to decompose urea in the absence of oxygen. Jacoby[25] obtained a dried preparation of the bacillus in which urease could be preserved for a long time and was active in the presence of toluol. Rubentschik found also that urea could be decomposed in the absence of the living organism and published a series of articles on six urea-splitting bacteria isolated by him from the soil.[26][27][28][29][30] Jacoby stated that leucin was necessary for the production of bacterial urease.[25][31] Takahata[32] found that the optimum reaction of Sorensen's solution for the urea decomposition of the proteus bacillus was pH 7·0 and that urease was extracted from the dried bacterial preparation by the neutral phosphate solution and its activity was favoured by the presence of glycocoll; Lehr[33] concluded that beryllium chloride increased the urease activity of the proteus bacillus in the phosphate buffer mixture. Thompson isolated the *Corynebacterium thompsoni* which is a strong urea-splitting organism and occurred in epidemic form in infected wounds and urinary fistulæ.[34]

The bulk of this historical survey, together with much of the bibliography was obtained from an article by M. Ishikawa. All the references listed here may be obtained in Sydney.

Technique.

Differentiation of Organisms.

Every culture was examined for its behaviour towards urea and if evidence of urea-splitting was obtained, the organism was differentiated as far as possible.

All coliform organisms which failed to split urea were inoculated into litmus milk, glucose broth (for acetyl-methyl-carbinol), lactose, glucose, maltose,

mannite, saccharose and dulcite. Attention was also paid to morphology and cultural characteristics. This is a rather more extensive differentiation than is carried out in all routine cases in the Royal Prince Alfred Hospital, and serves to separate the *genera*, but not all species.

The coliform organisms which split urea, were differentiated by the study of the following: morphology, cultural characteristics, motility, reaction to litmus milk, to gelatine, to glucose broth, to peptone water (for indol), to nitrate broth, to lactose, to glucose, to maltose, to mannite, to saccharose, to dulcite, to galactose, to glycerine, to xylose, to adonite, to lævulose, to inosite, to sorbite, to erythrite, to salicin, to arabinose, to raffinose, to inulin, to dextrin and to starch.

All cocci, whether urea-splitters or not, were examined for their morphology and their cultural characteristics were cultured in litmus milk, gelatine, peptone water and nitrate broth. The cocci were not inoculated into the sugars as a routine.

The following is a list of the various media used for differentiation and the times over which the action of the organisms were observed. If no action took place within the stated time, a negative result was recorded.

TABLE VIII.

Media.	Time
Litmus milk	Up to 15 days.
Motility	6, 12 and 24 hours (in glucose broth).
Urea	4 days.
Gelatine	21 days.
Glucose broth (acetyl-methyl-carbinol)	4 days.
Peptone water (indol)	4 days.
Nitrate broth	2 days.
Sugars	4 days.
Inspissated serum	21 days.
Pigment formation	21 days.

The Urea Indicator Medium.

At the commencement of the investigation the first task was to devise some simple medium in which all common organisms would grow readily, and which contained urea and some suitable indicator. Other essentials were that the medium should be easy to make in bulk, that it should keep well over a long period of time and that the protein base of the medium should be of constant composition and give a small and constant amount of ammonia from bacterial proteolysis.

Peptone water seemed to satisfy all requirements as a protein base. It was made up as follows:

Peptone (Witte): 1·0.
Sodium chloride: 0·5.
Water: 100·0.

No difficulty was found in obtaining good growth in this medium. Proteolysis gave an average of about one milligramme of nitrogen per five cubic centimetres. Kolle and Wassermann[35] give the figure 1·8 milligrammes of nitrogen in five cubic centimetres after a week. As three days was the limit of time used in the quantitative estimations in this investigation, the results are quite comparable. The final hydrogen ion concentration for coliform bacilli cultures approached closely to the figure given by Shohl,[36] namely pH 8·0. Also the buffer action of the medium between pH 7·0 and 9·0 was far lower than that of bouillon and therefore more suitable for the use of a dye indicator.

The next step investigated was the most suitable concentration of urea to be used in the medium; 0·5%, 1·0%, 2·0%, 3·0%, 4·0% and 5·0% of urea were tried and organisms were inoculated into tubes of each concentration. After twenty-four hours' incubation, one drop of a 10^{-4} dilution was spread on a Petrie plate and again incubated. In no instance was the growth so profuse as in the plain peptone water. However, the colonies were quite uncountable from the 0·5% and the 1·0% tubes, while the higher concentrations gave progressively fewer colonies as the concentration of urea increased. A percentage of 0·75% urea was decided on and proved perfectly satisfactory. It is worthy of note that this concentration corresponds fairly well with the concentration of urea in normal urine. Thus if the urea content of the blood be ten milligrammes per hundred cubic centimetres and Ambard's coefficient be 80, then there are 800 milligrammes of urea per hundred cubic centimetres of urine, that is 0·8%.

In the selection of a suitable indicator the following points were considered. A range from pH 7·0 to 9·0 at least was desirable. A bicolour indicator was more satisfactory than a monocolour indicator. This point was noticed early in the investigation. Urea medium had been made up with phenolphthalein as indicator. The reaction was adjusted to pH 7·0 before sterilization and after sterilization it was found that the reaction had become pH 8·3, while outwardly there was nothing to show that the reaction had changed. The indicator should not be easily bleached by organisms. The indicator should not inhibit bacterial growth.

Thymol blue, methyl thymol blue, phenolphthalein, cresol phthalein, thymol phthalein and thymol violet were tried and rejected. Thymol blue and methyl thymol blue proved unsuitable on two grounds; they were colourless at pH 7·0 and the blue colour was not sufficiently intense to overwhelm the yellow colour of the medium. Phenolphthalein gave excellent end-points and red was a better indicator colour than blue, but again it was colourless at pH 7·0. The same objections applied to cresol phthalein. Thymol phthalein and thymol violet had too low a range, pH 9·3 to 10·5 and pH 9·0 to 13·0 respectively.

The indicator which was finally chosen was the British Drug House "Universal Indicator." This is a compound indicator which has an effective range from pH 3·0 to pH 11·0. Without possessing the accuracy of a single indicator, it can be read without a comparator tube to within pH 0·5. This was found sufficiently accurate for the investigation. It gives a fine range of colour from pH 7·0 to pH

9·0. At pH 7·0 it is greenish-yellow, at pH 7·5 yellowish-green, at pH 8·0 green, at pH 8·5 blue and at pH 9·0 violet. This differs somewhat from the approximate colours given on the bottle label, but frequent controls with other known indicators showed that the colours given above are correct for peptone water. Thus it could be seen at a glance that the medium was at the correct hydrogen ion concentration for inoculation and had not degenerated from any cause. No difficulty was met with in its use; bleaching occurred on one occasion only and no appreciable inhibition of growth was caused by it. Ten cubic centimetres per litre of peptone water gave the most suitable depth of colour.

One precaution was always taken. After an organism had been incubated for four days, a drop of phenolphthalein in alcoholic solution was added. This showed immediately and conclusively whether the pH had reached 8·4 or not and checked any fallacy on the part of the British Drug House "Universal Indicator." This measure also insured that the hydrogen ion concentration of the medium was well on the alkaline side of pH 8·0, which Shohl[36] showed was the final reaction of all colon organisms when cultivated in a carbohydrate free medium. Wyeth[37] also showed that if the original reaction of the medium was lower than pH 8·48, proteolysis caused it to become more acid. Thus it was certain that the alkali produced by proteolysis alone was not capable of lowering the hydrogen ion concentration of the medium as far as pH 8·4. This was confirmed by inoculating many different strains of organisms into the medium without the urea. In no instance did it reach pH 8·4.

The criterion as to whether any given organism was a urea-splitter or not was made as follows: Any organism which when grown in 0·75% urea peptone water for ninety-six hours gave a pH of 8·4 or over, was regarded as a urea-splitting organism.

That this criterion was a true one was found by a subsequent series of experiments given below, in which the actual amount of urea split in a certain time by every organism which gave a positive indicator result, was estimated. Organisms not giving positive indicator results were also estimated and with one series of exceptions which were readily explained, not one anomalous result was recorded. That is to say, every organism which produced a pH of 8·4 or over in the urea peptone water medium, was proved by quantitative experiment to split urea, while those which failed to give a pH of 8·4, were definitely not urea-splitters.

It was also found experimentally that if all the urea contained in the medium were changed to ammonium carbonate, the reaction of the solution was about pH 8·7. Thus a strong coloration of the phenolphthalein showed that a considerable percentage of the urea had been decomposed. In no instance, even with large quantities of urea in solution, was a pH of less than 8·7 attained by means of bacterial urea-splitting. This is due to the fact that ammonium carbonate solutions have a constant alkalinity which lies between pH8·5 and pH 8·8. No determination of the hydrogen ion concentration of this salt had apparently been published and the above result gives two fairly close limits between which the reaction lies. It is a strong buffer salt, large quantities of sodium hydrate being required to make solutions more alkaline.

The final difficulty met with in the evolution of a suitable medium was the instability of urea in solution. If a urea solution is raised to 100° C. for a prolonged period, decomposition occurs and the solution becomes definitely alkaline. This is due to the partial transformation of urea at this temperature into ammonium cyanate.[38] It was found that if the indicator were added before sterilization and the reaction adjusted to pH 7·0, a quarter of an hour in the steamer did not produce excessive decomposition. Usually the pH on removal was about 7·5. Incubation tested the sterility and incubation at 37° C., even if prolonged, did not seem to produce any further decomposition. Thus it was found impossible to produce a urea medium which before inoculation was ammonia free. However, the amount of ammonia present in any batch of medium before inoculation could be readily estimated and allowance made in the final calculations. All media showing a lower pH than 7·5 after sterilization were rejected.

Quantitative Estimations.

In order to complete the investigation of the urea-splitting organisms it was determined to attempt a quantitative estimation of the amount of urea split in a certain time by all those organisms which give a positive indicator result on culture. Early attempts met with failure owing to the ammonia either evaporating from the test tube through the cotton wool plug or else through the ammonia forming compounds with the amino-acids of the peptone during incubation. In either event the results were very low and it was obvious that there was more ammonia formed than appeared in the titration. Rubentschik[26] met with the same difficulty and overcame it by a double titration. First he titrated the amount of ammonia present in the inoculated incubated culture tube; then taking a second tube containing an equal amount of medium and inoculated with the same organism and incubated for a similar period, he completed the urea splitting with soy bean urease and again estimated the ammonia formed. Suppose that there were originally fifty milligrammes of urea in each tube and the second titration gave a result of forty milligrammes of urea; it is obvious that there is a loss of ten milligrammes of urea. This loss must have taken place after the urea had been split into ammonia, since undecomposed urea is not volatile, and forms no compounds with other constituents of the medium. The result of the first titration will give the total amount of ammonia remaining in the medium and if the deficiency of ammonia as revealed

by the second titration is added to this figure, the result will give a true indication of the amount of urea which has been decomposed.

Certain other sources of error must also be controlled. One which will tend to raise the amount of urea split by the organism is the presence of ammonia in the medium due to the proteolytic action of the bacteria on the peptone. A second and much greater source of error will be due to the ammonia present in the medium due to the degeneration of the urea during sterilization.

These sources of error were controlled as follows. Urea-splitting organisms were inoculated into peptone water together with the indicator, but containing no urea. A remarkably even series of results given in Table IX gave a maximum of 2% to be allowed for the proteolytic action. In no instance was the proteolytic action alone sufficient to produce colour in phenolphthalein. As it has been pointed out before, the final reaction of cultures of *Bacillus coli* in sugar free medium lies very close to pH 8·0.

Table IX.

Serial Number of Urea-splitting Organism.	Urea Equivalent in Milligrammes in 5 c.cm. of Peptone Water containing No Urea.
5	0·15
7	0·90
8	0·90
10	1·08
11	1·11
47	1·11
66	0·30
71	0·99
87	0·45
149	0·99
157	0·21
168	1·29

Average amount of proteolytic ammonia is equivalent to 0·79 milligramme of urea in five cubic centimetres, while the maximum is 1·29 milligrammes of urea. Experiments were done in peptone water urea medium which contained fifty milligrammes of urea per five cubic centimetres. So these results must be doubled in order to obtain the percentage error to be allowed for. The average error due to proteolytic ammonia was 1·58%, while the maximum was 2·58%.

The second and much greater source of error was controlled as follows. Many tubes of peptone water urea medium were estimated both with and without the addition of soy bean urease. These tubes were uninoculated and were taken at random from each batch of medium as it came from the sterilizer. Results as shown in Table X gave the amount of urea which had degenerated in sterilization and incubation, and which could not be attributed to any effect of the organisms which were to be investigated in the medium.

Table X.

Batch.	Urea Equivalent in Milligrammes. No Urease Added. Average of Six Estimations.	Urea Equivalent in Milligrammes. Urease Added. Average of Six Estimations.	Percentage of Urea Degenerated in Sterilization.
A	3·9	45·6	16·6
B	1·5	45·0	13·0
C	1·4	42·2	18·4

These and all the quantitative estimations were performed in five cubic centimetres of urea peptone water, containing 1% urea; that is five cubic centimetres contain fifty milligrammes of urea and the results must be doubled to obtain percentages.

As a final control a series of organisms which had failed to split urea in the indicator tubes, were inoculated into urea medium and the results quantitatively estimated as before. These organisms were cultivated in Batch C of the medium and it will be seen from Table X how closely these last results correspond with the sum of the results obtained from Tables IX and X.

Table XI.

Serial Number of Organism.	Urea Equivalent in Milligrammes. No Urease Added.	Urea Equivalent in Milligrammes. Urease Added.	Percentage of Urea apparently split by Organism.
130	1·8	42·9	17·8
141	1·8	42·9	17·8
147	2·1	44·4	15·4
173	1·8	42·6	16·4
184	1·5	43·8	15·4
190	2·7	43·5	18·4
191	2·1	42·0	20·2
198	2·1	44·4	15·4
204	1·5	45·0	13·0

These results range from 13·0% to 20·2%, with an average of 16·6%.

It is seen, therefore, that in estimating the percentage of urea split by those organisms which gave positive indicator results 20% must be subtracted from the estimated figure. It should be noted how closely these percentages agree in organisms which have been placed in the various groups. It is almost without exception that if one member of a group ferments urea strongly, all the rest will do so too and *vice versa*.

Finally, it should be mentioned that two groups of organisms showed a considerable degeneration of their urea-splitting ability after cultivation for some time on artificial media. As the organisms arrived at the laboratory they were obtained in pure culture and then differentiated into urea-splitters and non-urea-splitters. The urea-splitters were then fully differentiated as described above and the non-urea-splitters were partially differentiated. After differentiation all the organisms were kept in stock culture until the whole 211 organisms in the series had been investigated. It was not until this had been done that quantitative estimations were made and as the collection of the organisms took some months, the earliest collected had been on artificial media and subcultured many times during this period. Geilinger[39] draws attention to this. He says: "A sample of the unstable behaviour is found in the tribe 'soil A'; in the course of a few months it lost its ability to split urea in a 10% concentration."

Thus two of the groups met with fermented urea quite strongly when first cultured, but when a quan-

titative estimation was made after a few months they failed completely to split urea. If these failures had been sporadic throughout the whole series, doubt must have been thrown upon the reliability of the indicator method of determining the urea-splitting property. However, the organisms concerned fall into definite groups and thus give a favourable rather than an unfavourable impression that the results are true ones and that the method of classification is correct.

An attempt was made to reeducate the organisms of type A, subtype 1, to split urea again. After subculturing on twenty occasions in urea peptone water medium there was still no evidence of urea-splitting.

In the quantitative estimations of the urea-splitting organisms the method of Van Slyke and Cullen[40] was used throughout. The urease was obtained in the tablet form from Hynson, Westcott and Dunning.

Results.

Source of Material.

Out of 211 cultures examined 200 were obtained from infected urine. The remaining eleven were organisms obtained from various stock strains belonging to the Commonwealth Serum Laboratories. These included five strains of proteus, five species of salmonella and one *Eberthella typhi*. Special care was taken throughout the investigation to avoid duplication of results; there are not more than one or two instances where the same patient has supplied more than one culture.

Extent of Investigation.

Sixty organisms were differentiated as far as possible and of the remainder all but eleven were partially differentiated. The eleven which were undifferentiated, consist mainly of non-urea-splitting organisms which were met with early in the investigation before the technique was standardized. Two urea-splitting cocci were among those undifferentiated.

Proportion of Urea-splitting Organisms.

Out of 211 cultures, fifty-four were found to split urea, that is 25·6%. Of the fifty-four urea-splitting organisms twelve were cocci and forty-two were bacilli, that is 28·5% of the urea-splitting organisms were cocci. As against this result, out of the total 211 cultures only thirty-one were cocci, that is 14·7%. From these figures it is seen that the property of splitting urea is relatively more frequent among the cocci than among the bacilli. To put the matter in a slightly different manner, 38·7% of all the cocci examined were found to split urea; only 23·3% of all the bacilli examined were able to split urea.

Nature of Organisms Investigated.

Excluding the fifty-four urea-splitting organisms which will be dealt with in detail in another section, there were nineteen cocci and 138 bacilli.

The cocci were all Gram-positive and their cultural reactions may be examined in Table XII. It will be seen that they show a great variation in type and are not easily classified according to Bergey's "Manual of Determinative Baeteriology." About half showed the cultural appearances of the genus *Micrococcus* and the other half were more like members of the genus *Staphylococcus*.

TABLE XII.

Serial Number.	Type of Culture.	Litmus Milk.			Gelatine. Liquefaction.	Indol.	Nitrites.
		Alkaline.	Acid and Clot.	Acid.			
86	Micrococcus like	1, 3, 15	–	–	–	–	–
123		1, 3, 15	–	–	–	–	–
206		1, 3, 15	–	–	–	–	–
120	Staphylococcus like	1, 3, 7	–	–	–	–	+
121		–	1	–	–	–	+
134		–	1	–	–	–	+
139		1	7	3	–	–	+
155		–	1	–	–	–	+
192		–	1	–	–	–	+
122	Micrococcus like	1, 3	5	–	–	+	+
201		–	1	–	–	+	+
133	Micrococcus like	1, 3, 7	–	–	+	–	+
175		1	3	–	+	–	+

The remaining six non urea-splitting cocci were undifferentiated.

The remaining six non-urea-splitting cocci were undifferentiated.

All the non-urea-splitting bacilli, 138 in number, were Gram-negative. By reference to Bergey they were classified as follows:

Escherichia coli communis	35
Escherichia coli communior	30
Escherichia acidi tactici	9
Aerobacter aerogenes	12
Eberthella typhi	4
Salmonella (various)	5
Alcaligenes fæcalis	6
Pseudomonas (various)	7
Miscellaneous (unidentified)	30
Total	138

Of the seven cultures of *Pseudomonas*, only three were identified as *Pseudomonas aeruginosa*. These three were quite typical and not only coincided with Bergey's table, but also with the gelatine liquefying organisms in Lilley's Table.[41] The remaining four were evidently another variety of *Pseudomonas*. Pigment formation was very slow both in solid and liquid media, taking about three weeks to appear. Two of them liquefied gelatine slowly and the other two failed to liquefy it in three weeks. Inspissated serum was slowly liquefied by all four; all reduced nitrates to nitrites and pep-

tonized litmus milk, but one failed to acidify glucose. These organisms were only recognized as members of the *Pseudomonas* genus during the routine reinoculation of old cultures when the pigment formation was seen.

Clinically the patients suffering from this infection had mild chronic pyelitis which cleared up rapidly with free fluids and pelvic lavage. Table XIII shows their cultural reactions.

TABLE XIII.

Serial Number.	Cultural Characteristics.	Litmus Milk.	Motility.	Gelatine. Liquefaction.	Nitrites.	Glucose.	Inspissated Serum. Liquefaction.	Pigment Formation. Green.
49	Spreading	Alk. (pept.)	+	+	+	A	Rapid	Rapid
83	Spreading	Alk. (pept.)	+	+	+	–	Rapid	Rapid
153	Spreading	Alk. (pept.)	+	+	+	A	Rapid	Rapid
28	Not spreading	Alk. (pept.)	+	–	+	A	Slow	Slow
59	Not spreading	Alk. (pept.)	+	+	+	A	Slow	Slow
128	Not spreading	Alk. (pept.)	+	+	+	A	Slow	Slow
211	Not spreading	Alk. (pept.)	+	–	+	A	Slow	Slow

It is of interest that great instability was noticed in the behaviour of organisms which in every way were similar to *Escherichia coli communior* or *Aerobacter aerogenes* in their production of acetyl-methyl-carbinol. Those that yielded carbinol reactions were approximately equal in number to those that did not yield this reaction. Bergey gives carbinol "positive" as being a general characteristic of the genus *Aerobacter*; also *Escherichia coli communior* does not produce carbinol according to this author. It appears, therefore, that this test does not warrant the importance which Bergey lays upon it, as a general difference between *genera*.

The majority of the organisms under the heading miscellaneous was Gram-negative bacilli which formed no gas in sugars, did not liquefy gelatine and could not be identified in Bergey's classification. They were associated with chronic bacilluria, pyelitis *et cetera* and showed no general systemic effects. They corresponded most closely with that group of organisms classified by Muir and Ritchie[42] as *Bacillus coli anaerogenes*.

The Urea-Splitting Organisms.

Thirty-four urea-splitting organisms were isolated during the investigation. Twelve were cocci and forty-two were bacilli.

The urea-splitting cocci proved most difficult to identify. Some were in all respects similar to the *Staphylococcus albus*; others showed more of the characteristics of the genus *Micrococcus* and grew in shiny greyish or brownish colonies. Eleven of the series were Gram-positive and were weak urea-splitters which tended to lose their power of urea fermentation after cultivation on artificial media. The twelfth was a Gram-negative cocco-bacillus which fermented urea strongly, was non-motile and did not yield reactions to all other tests. It grew readily on ordinary nutrient agar, but showed a tendency to die out in stock culture rather soon. The cultural reactions of the cocci are given in Table XIV, the classification being very unsatisfactory owing to the diversity of their cultural characteristics and to the small number of organisms isolated. At least one hundred different strains would be required to enable them to be fitted into a proper scheme of classification.

TABLE XIV.

Serial Number.	Cultural Characteristics.	Litmus Milk.		Urea.	Gelatine. Liquefaction.	Indol.	Nitrites.	Staining.	
		Acid.	Acid and Clot.					Gram-positive.	Gram-negative.
				%					
5	Micrococcus like, sticky grey or brown colonies	15	–	10·4	–	–	–	+	–
13		15	–	18·8	–	–	–	+	–
18		15	–	7·4	–	–	–	+	–
66		–	–	13·4	–	–	–	+	–
74		–	–	9·8	–	–	–	+	–
154		7	–	6·2	–	–	–	+	–
27	*Staph. albus* like	–	–	35·2	–	–	+	+	–
105		–	–	18·4	–	–	+	+	–
33	*Staph. albus* like	–	1	3·2	+	–	+	+	–
37		–	15	8·0	+	–	+	+	–
157	*Staph. albus* like	15	–	58·4	–	–	–	–	+

The bacilli forty-two in number and all Gram-negative were far more satisfactory to deal with than the cocci. Without exception they fell naturally into clearly defined groups which closely corresponded not only in their cultural characteristics, but also in their quantitative urea-splitting ability. Before discussing the groups in detail a few generalizations may be made.

Without exception every organism which ferments urea strongly, liquefies gelatine. Those organisms which fail to liquefy gelatine, even though they closely correspond to the gelatine liquefiers in all other respects, are only comparatively feeble urea-splitters and also show a tendency to lose their urea-splitting properties when cultivated for some time on artificial media. Another almost universal observation is their motility. With the exception of one group all the stronger urea-splitters were actively motile. A few were weakly motile or else tended to lose their motility very rapidly, but there was not one organism isolated which could be definitely classed as non-motile. Every organism reduced nitrates to nitrites and all but one fermented carbohydrates with the production of acid and gas; the exception to this rule produced acid only.

A generalization can also be made from a second standpoint. First, all non-lactose fermenters which give the cultural characteristics of the genus *Proteus*, ferment urea; all but one sub-group of these ferment urea strongly. Secondly, there are several groups of organisms, all members of which seem to fail to split urea. Outstanding are the *Escherichia coli communis, Escherichia acidi lactici, Eberthella typhi*, the salmonella group, the *Alcali-*

genes fæcalis group and the *Pseudomonas* group. It is also doubtful if the *Aerobacter* group has any influence upon urea. On the evidence acquired in this investigation it appears that the *Aerobacter aerogenes* proper has no effect upon urea, but a close relative which however fails to produce carbinol, ferments urea quite strongly.

It should be mentioned here that the *Corynebacterium thompsoni*, a strong urea-splitting organism and an inhabitant of urinary fistulæ, was not met with during the investigation.

The following key (after Bergey) may make the classification of the urea-splitting bacteria more clear.

Urea-Splitting Bacilli.

Gram-negative rods, all growing well on arficial media; they generally attack carbohydrates with the production of acid and gas. All ferment urea forming ammonium carbonate.

Key to Groups.

A. Form acid and gas in carbohydrates.
  1. Acid and gas in lactose.
    a. Acid and gas in dulcite ..... Type A
    b. No acid or gas in saccharose ..... Type B
      aa. No acid or gas in dulcite ... Type C
  2. No acid or gas in lactose ..... Type D
B. No gas but only acid in carbohydrates ..... Type E

Type A is an interesting group which consists of two subtypes.[1] These are distinguished by two factors. One subtype liquefies gelatine rapidly and ferments urea strongly, while the other subtype fails to liquefy gelatine and ferments urea comparatively weakly. Also it was found that the latter loses its power of fermenting urea altogether after being cultivated for some time on artificial media. The appearance of these two subtypes on the agar slope is also quite different. Subtype 1 gives a thick, white, shiny, opaque colony with slightly scalloped edges; subtype 2 gives a colony which is far less opaque and is thinner; it has a distinct tendency to spread over the surface of the media in the same way as *Proteus*.

Notable features about both subtypes are the consistency of their agar reactions and also the fact that without exception all produce carbinol. Subtype 1 was also culturally identical with another group which failed to ferment urea. This group of organisms could not be classified in accordance with Bergey's tables. Here it has been included among the *Escherichia coli communior* strains, but it possesses the important distinction that it produces acetyl-methyl-carbinol. In addition the colonies on solid media are different in appearance. *Echerichia coli communior* grows in a grey-brown, somewhat translucent colony, while the unknown organism forms a thick, white, slimy colony with scalloped edges. In fact, it seems that they are really members of the same group, but that some strains have developed the ability to ferment urea.

It will be noted that with the one exception of the positive carbinol reaction that subtype 1 shows a remarkable resemblance to *Escherichia coli communior*. It was thought at first that these organisms might be a development of *Escherichia coli communior*, where the ability to produce carbinol had developed alongside the ability to split urea. This is uncertain, however, because the carbinol showed no doubtful readings, it was either strongly positive or completely "negative." On the other hand, the urea splitting property showed all grades from a complete inability up to quite strong powers of fermentation.

It seems, therefore, that Type A is very similar culturally to the *Escherichia coli communior*, but is definitely a different species. It differs in the production of carbinol and the fermentation of urea and has a subtype which possesses very strong urea-splitting properties and also liquefies gelatine.

Type B is a strong urea-splitter of which only three strains were isolated. On the agar slope its colonies are translucent, thin and spread like proteus. It is actively motile and in many ways seems to be closely related to the *Escherichia coli communis*. The most important differences, however, are the proteus-like appearance of the colonies and also the fact that it liquefies gelatine. In addition no true *Escherichia coli communis* possesses the ability to ferment urea. In a series of thirty-five strains all failed to ferment urea.

Type C is best regarded as consisting of three subtypes. Subtype 1 is a strong urea-splitter, its colonies spread like proteus; all members liquefy gelatine and it often gives doubtful or positive carbinol reactions. In its carbohydrate reactions it differs from strain to strain, but on the whole resembles the *Aerobacter aerogenes* more than any other organism. The carbinol reactions, however, are very variable.

Subtype 2 is almost identical with subtype 1, but it forms acid and gas in dulcite. If the key is consulted, it will be seen that this type C has been classified under the heading "No acid or gas in dulcite." In spite of this, however, this organism can be placed nowhere as well as here. Elsewhere the sugar reactions are quite anomalous on comparison. Only one strain in this subtype was isolated. It ferments urea and liquefies gelatine powerfully.

Subtype 3 corresponds with subtype 1 except that the culture on solid media does not spread, that gelatine is not liquefied and that urea is not split so strongly, this power being completely lost on prolonged cultivation on artificial media.

All the members of Type D are non-lactose fermenters and of these no less than fifteen strains were obtained. Five were supplied by the Commonwealth Serum Laboratories and the remaining ten were cultured from urine during the investigation. They fall easily into four subtypes.

[1] In this discussion the terms genus and species have been purposely avoided. It is impossible at this stage to say whether the urea-splitting organisms form a bacteriological genus or whether they are merely species of existing *genera*. It is hoped that more routine work on this subject may decide the question and place these organisms in their correct places in a bacteriological classification.

TABLE XV.

Serial Number.	Type of Culture.	Litmus Milk.	Motility.	Gelatine.	Carbinol.	Indol.	Nitrites.	Lactose.	Glucose.	Maltose.	Mannite.	Saccharose.	Dulcite.	Galactose.	Glycerine.	Xylose.	Adonite.	Lævulose.	Inosite.	Sorbite.	Erythrite.	Salicin.	Arabinose.	Raffinose.	Inulin.	Dextrin.	Starch.	Urea Qualitative.	Urea Quantitative.	Time (Days).
																													%	
	Type A.																													
	Subtype 1.																													
42	Thick, white, slimy, glistening; with scalloped edges and no tendency to spread	1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	+	–	3
64		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	++	–	3
87		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	++	–	3
94		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	++	–	3
107		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	++	–	3
180		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	AG	++	–	3
199		1 AC	±	–	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	A	–	+	–	3
	Subtype 2.																													
10	Proteus like	1 AC	+	liq.	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	+	32·0	3
12	Proteus like	1 AC	+	liq.	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	–	–	+	22·4	3
186	Proteus like	1 AC	+	liq.	+	–	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	AG	+	48·8	3
	Type B.																													
11	Colonies show a tendency to spread like proteus	1 AC	+	liq.	–	+	+	AG	AG	AG	AG	–	AG	AG	AG	AG	–	AG	–	AG	–	–	AG	–	–	–	–	+	54·8	3
55		3 AC	+	liq.	–	+	+	AG	AG	AG	AG	–	AG	AG	AG	AG	–	AG	–	AG	–	–	AG	AG	–	–	–	+	41·6	3
200		1 AC	+	liq.	–	–	+	AG	AG	AG	AG	–	AG	AG	AG	AG	–	AG	–	AG	–	A	AG	AG	AG	A	A	+	51·6	3
	Type C.																													
	Subtype 1.																													
6	Proteus like	3 AC	+	liq.	–	–	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	AG	AG	–	AG	–	–	–	AG	–	+	9·2	3
7	Proteus like	5 AC	+	liq.	–	–	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	AG	AG	–	AG	–	–	–	AG	–	+	33·8	3
124	Proteus like	1 AC	+	liq.	–	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	AG	–	–	AG	AG	–	–	–	+	36·8	3
135	Proteus like	1 AC	+	liq.	–	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	AG	–	AG	AG	AG	–	–	–	+	26·6	3
142	Proteus like	1 AC	+	liq.	–	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	AG	–	AG	AG	AG	–	AG	–	+	36·8	3
149	Proteus like	1 AC	+	liq.	±	–	+	AG	AG	AG	AG	AG	–	AG	AG	–	–	AG	–	AG	–	–	–	–	–	AG	–	+	28·4	3
156	Proteus like	1 AC	+	liq.	+	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	AG	–	AG	AG	AG	AG	–	–	+	29·4	3
159	Proteus like	1 AC	+	liq.	–	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	–	AG	–	AG	–	–	–	–	–	+	47·6	3
177	Proteus like	1 AC	+	liq.	+	+	+	AG	AG	AG	AG	AG	–	AG	AG	AG	–	AG	AG	AG	–	–	–	–	–	–	–	+	31·4	3
	Subtype 2.																													
71	Proteus like	3 AC	+	liq.	–	+	+	AG	AG	AG	AG	AG	AG	AG	AG	AG	–	AG	–	AG	–	–	AG	–	–	–	–	+	29·8	3
	Subtype 3.																													
152	White, discrete colonies, not spreading	3 AC	+	–	–	–	+	AG	AG	AG	AG	AG	–	AG	AG	AG	AG	AG	–	AG	–	AG	AG	AG	–	–	–	++	–	3
164		3 AC	+	–	–	–	+	AG	AG	AG	AG	AG	–	AG	AG	AG	AG	AG	–	AG	–	AG	AG	AG	–	–	–	++	–	3

A = acid. AG = acid and gas. AC = acid and clot.

TABLE XV (*Continued*).

Serial Number.	Type of Culture.	Litmus Milk.	Motility.	Gelatine.	Carbinol.	Indol.	Nitrites.	Lactose.	Glucose.	Maltose.	Mannite.	Saccharose.	Dulcite.	Galactose.	Glycerine.	Xylose.	Adonite.	Lævulose.	Inosite.	Sorbite.	Erythrite.	Salicin.	Arabinose.	Raffinose.	Inulin.	Dextrin.	Starch.	Urea Qualitative.	Urea Quantitative.	Time (Days).
			Type D.																										
Subtype 1.																													
8	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	% 33·2	3
47	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	35·6	3
62	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	A	–	A	–	–	–	–	–	–	–	–	–	32·0	3
76	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	17·6	3
167	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	50·0	3
168	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	49·4	3
170	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	48·8	3
171	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	35·0	3
174	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	–	–	–	–	AG	AG	AG	–	A	–	–	A	–	–	–	–	–	A	33·2	3
188	Proteus like	3 Alk. (Peptonized)	+	liq.	–	+	+	–	AG	AG	–	AG	–	AG	AG	AG	A	AG	–	–	–	–	–	–	–	AG	A	32·0	3
Subtype 2.																													
137	Discrete white colonies, not spreading	3 Alk. (Peptonized)	+	–	–	+	+	–	AG	–	–	–	–	AG	–	–	–	AG	–	–	–	–	–	–	–	–	–	–	3
Subtype 3.																													
61	Proteus like	3 Alk. (Peptonized)	++	liq.	–	++	++	–	AG	AG	–	AG	–	AG	A	A	–	A	AG	–	–	–	AG	–	–	–	–	–	15·2	3
169	Proteus like	3 Alk (Peptonized)	++	liq.	–	++	++	–	AG	AG	–	AG	–	AG	A	AG	–	A	AG	–	–	–	AG	–	–	–	–	–	34·6	3
Subtype 4.																													
54	Proteus like	3 AC	++	liq.	–	–	++	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	33·2	3
140	Proteus like	3 AC	++	liq.	–	–	++	–	AG	–	–	–	–	AG	AG	AG	–	AG	–	–	–	–	–	–	–	–	–	29·0	3
			Type E.																										
187	Non-spreading, greyish-brown	15 Alk.	+	–	–	–	+	–	A	–	A	–	–	A	–	–	A	A	A	–	–	A	–	–	–	–	–	% 13·2	3

A = acid. AG = acid and gas. AC = acid and clot.

Subtype 1 is the largest; it has ten representatives and is somewhat heterogeneous, in fact it might be still further subdivided. However, it is constant in many important characteristics. All members have the typical proteus-like spreading culture on solid media. They peptonize litmus milk strongly, all are actively motile, they ferment urea strongly, they liquefy gelatine and they do not form indol. Their sugar reactions vary somewhat, but none ferments lactose.

Subtype 2 has one representative and is characterized by four features. It is a weak urea-splitter which loses this property completely after cultivation for some time on artificial media; its colonies are white and fairly discrete and do not spread; it fails to liquefy gelatine and it forms indol.

Subtype 3 has two representatives. These are similar to subtype 1 in all respects, save that they produce indol in peptone water medium. They ferment urea strongly.

Subtype 4 differs from subtype 1 also in only one respect; it rapidly forms acid and clot in litmus milk. The members of this subtype are strong urea-splitters, but do not seem to be quite so powerful as the members of subtype 1.

There can be no doubt that type D represents the *Proteus* genus which has been known as a powerful urea-splitter for a long time.

Type E is quite different from all the other bacilli in that it is a fairly strong urea-splitter, does not liquefy gelatine and forms no gas in carbohydrates. It reduces nitrates to nitrites and forms acid in glucose, mannite, galactose, adonite, lævulose, inosite and salicin. In the absence of further information it can only be placed in the *Bacillus coli anaerogenes* group of Muir and Ritchie.

Conclusions.

1. Very little work has been done on the urea-splitting organisms which cause infected phosphaturia.

2. Urea peptone water combined with the British Drug House "Universal Indicator" proved most suitable for the separation of those organisms which split urea from those which did not.

3. Many varieties of Gram-positive cocci and Gram-negative bacilli were found to have well developed powers of splitting urea.

4. Apart from their urea-splitting property, there is no other single constant factor in the organisms examined.

5. The number of cocci isolated was too small to enable a classification to be made.

6. The bacilli fell into five well defined groups, four of which could not be identified with any organism previously described.

7. All those bacilli which fermented urea strongly, gave cultures similar in appearance to proteus and all liquefied gelatine.

8. Those bacilli and cocci which only fermented urea weakly, lost this property altogether when grown for some time on artificial media.

9. All bacteria cultured from urine should be routinely examined for their urea-splitting properties.

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Reviews.

THE ETERNAL QUESTION.

MRS. AUGUSTA GASKELL has written a book in which she elaborates her hypothesis of the nature and mechanism of life. Having enunciated a physical hypothesis, she converts it into a theory and before she completes the two hundred and eighty-seventh page she transforms it into something approaching an unchallengeable truth. "What is Life?" starts with an introduction by Professor Karl T. Compton, Professor of Physics of the Princeton University, in the course of which he states that Mrs. Gaskell gives an accurate account of the modern doctrines of the physics of the atom.[1] He finds that the physicist must admit that he knows of no independent experimental evidence to suggest or to support her hypothesis. Professor Raymond Pearl, Professor of Biology of the Johns Hopkins University, also contributes an introduction. He writes that in a sense all of the specifically biological chapters in which the biological implications and consequences of the theory are discussed, are premature. He adds that if the theory is not true, the discussions are idle. Even if the thesis be true, as ancillary evidence the discussions in his opinion have but little weight.

We may confess that Mrs. Gaskell prejudices her chances of a sympathetic reception of her doctrine by three bad faults. The first is an irritating reiteration of a statement which is purely hypothetical and quite devoid of physical or other proof. The statement appears not twice or thrice, but very many times. It is varied occasionally, but is essentially the same conception despite its varied forms. It is a mistake to assume that an hypothesis gains in weight or becomes more acceptable because it is repeated. The second fault consists in the unrestrained use of italics. Long passages and short sentences are printed in italics on almost every page. We presume that the intention is to emphasize the passages, sentences or words. To the scientific reader it fails in this purpose and leaves the impression that the authoress, fearful lest she cannot secure adhesion to her views, endeavours to create an artificial importance for her statements. It is easy to emphasize an important statement without typographical aid. Clear enunciation, sound argument and the avoidance of redundant words always suffice. The third fault is one that makes the reading of the book difficult. Mrs. Gaskell has put forward an ingenious hypothesis, speculative, possibly fanciful; she rides her doctrine to death and then starts to build on an unproven hypothesis a superstructure that cannot be supported on so insecure a foundation. It matters little whether authorities are quoted by the page; other opinions, other conceptions weaken rather than strengthen an argument based on dogmatic statements that are at present incapable of demonstration or of scientific proof.

The first fifty pages of the book are devoted to quite a good account of Rutherford's doctrines of the structure of the atom and of the Bohr-Sommerfeld theory of the atom. A great deal of detail unnecessary for her suggestions is given. In fact the modern physicist will scarcely accept her account of atomic physics as a specially reliable one, while the biologist, the biochemist and the biophysicist will prefer to consult the works of the eminent authorities quoted than to accept this revised version. She could have stated in a few pages the points in the modern doctrines of the structure of the atom on which her argument is founded. It must not be forgotten that only part of these doctrines can be presented as fact. Every year some parts of the current theories are being challenged and discarded in favour of fresh ideas. Be this as it may, she asks her reader to accept the hydrogen ion as a planetary system in which the planets are negative electrons which revolve around the nucleus. The ions are in a state of critical concentration. The hydrogen atom comprises two nuclei with a positive charge and one so-called orbit electron with a negative charge. The two positive ions repel one another, but are held together by the orbital electron. She suggests that an ion in the outer orbit of an atom takes a path from the interior to the periphery and is then ready to be parted from the atom. If a negative electron gets into the field of the positive hydrogen nucleus with its orbital electron at aphelion, the electron may be drawn into the field of the hydrogen ion in such a way that it will complete the hydrogen molecule or it may unite with the positive electron to form a normal hydrogen atom in which circumstances the negative electron will revolve about the positive electron at some distance. Physicists admit that these events may occur. Mrs. Gaskell goes a step further. She postulates that the onrushing negative or orbital electron may collide with the positive electron and form with it an exceedingly close union. It must be pointed out that there is nothing known to support such an event. It would be strange if it took place and in view of the uncertainty of the structure of the hydrogen atom it is hazardous to speculate on a pure guess without any guiding observation, direct or indirect evidence to support the conception. Allowing that this guess may be true, we can follow Mrs. Gaskell a little further. She states that the resulting unit, though it consists of the same units that constitute the hydrogen atom, would not be a hydrogen atom. The new unit could not enter into combination with atoms after the manner of the hydrogen atom, not having the mechanism of the hydrogen atom. What evidence is there in support of such an assertion? She continues by making a number of assertions concerning this alleged new unit, each one being stated and restated in different words. She persuades herself that this new unit becomes an intraatomic quantity, by reason of its peculiar constitution, its erratic path and its peculiar electromagnetic properties. Having allowed her imagination to devise this ingenious plot, she would have been wise had she awaited investigation to give a lead as to whether or not such an astounding proposition actually corresponds with fact. But she is impatient. She proceeds to postulate that a dual system is formed. It is made up of a material system, built of atoms, and an immaterial system, not "patterned after the manner of the chemical elements." She calls the material system the *Y* system and the immaterial system the *Z* system. She maintains that the *Z* quality, the intraatomic system, in equilibrium with the *Y* system imparts life. In other words *Z* is life.

[1] "What is Life?" by Augusta Gaskell, with an Introduction by Karl T. Compton and Raymond Pearl; 1928. London: Baillière, Tindall and Cox. Royal 8vo., pp. 324. Price: 16s. net.

When something happens to disrupt the dual system, life ceases and death results. She does not stop here. On page after page she postulates the same extraordinary hypothesis, gradually adding one, two, three and many more additional claims, continued from the same starting point, often without apparent logical connexion, until she has built up so complicated a formula that the reader might question whether she is serious. For example, she states: "The origin of life on the earth was due to a local condition of a critical concentration of ions that, owing to the constitution and the dynamics of the atom and the electron, necessitated the setting up of new equilibrium conditions which resulted in the origin of the dual system, living matter. This condition, . . . the condition of a critical concentration of ions, following trauma or other injury to cell structure, is the cause of cancer and of other neoplasms."

Mrs. Gaskell explains to her own satisfaction individuality, heredity, intellectual qualities, mental processes and much more. We have no space to follow her through her ramblings. When she states toward the end of her extraordinary book that her "theory" is well supported, we would reply that she has not enunciated a theory at all. She has added an unlikely hypothesis on a likely hypothesis and has permitted her imagination to fill many pages with words. Even the compositors and proof readers must have tired of her repetitions, for there are many typographical mistakes in the last chapter, although the earlier chapters are free from such errors.

CHEMICAL PHYSIOLOGY.

IN the preparation of the twelfth edition of his "Essentials of Chemical Physiology" Halliburton has had the collaboration of J. A. Hewitt and W. Robson.[1]

There must always be some difference of opinion on what ought to be included in a book which aims at giving the essentials of a subject. In such a text book, however, the inclusion of matters of historical interest only is unnecessary, while the use of an obsolescent terminology, as in the section of fats and lipoids, is undesirable. Now that quantitative determinations of many constituents of the blood are part of the daily routine of any efficient hospital, surely the treatment of this part of the subject ought not to be restricted to a description of a method for the determinations of blood sugar.

The sections on the respiratory functions of the blood and on the urine and many other sections are much more adequately treated. Because of these and because this text book gives a good deal of information about the properties of substances which tends to be skimped in some recent books, there is no doubt that it will fulfil the hopes of its authors and "continue its career of usefulness."

A SPECIAL CHAPTER OF SURGERY.

THOUGH primarily intended for medical practitioners in the tropics, a book entitled "Surgery in the Tropics," by Sir Frank Powell Connor,[2] contains a great deal of useful information to those practising in temperate climates. It could with advantage be read by surgeons and general practitioners in the northern parts of Australia and in the mandated territories and by men who have had little or no experience of the tropics and who may be tempted by the lure of travel to visit the Pacific islands or some of the remoter parts of the Commonwealth. In his preface the author states that "no attempt has been made to supplement the teaching which is laid down in an ordinary text book of surgery, such as that by Romanis and Mitchiner; nor does it enter into competition with such excellent text books of tropical medicine as that of Manson."

The first five chapters are the least interesting to practitioners in non-tropical regions. The numerous diseases mentioned in these chapters are with but few exceptions rarely if ever met in Australia, for example, plague, glanders, yaws, leishmaniasis, the many tropical granulomata and the tropical fevers such as trypanosomiasis, kala-azar. Leprosy and malaria are, of course, still encountered in many parts.

The ensuing six chapters deal with the dysenteries, amœbic, bacillary and bilharzial. The detailed descriptions of the various forms of amœbiasis and of bacillary dysentery, their ætiology, pathology, clinical features, diagnosis and treatment of their surgical complications leave little to be desired. The chapter on amœbic hepatitis and liver abscess is a masterly one; it is full and instructive.

The following five chapters contain information concerning schistosomiasis and more on filariasis. There are well illustrated sections on elephantiasis and the radical treatment of tropical hydrocele.

The final two chapters are devoted to a brief account of various intestinal trematodes and parasitic worms and of the bites of some vertebrate and invertebrate animals.

The book has a useful index and an appendix. It is amply illustrated.

INFECTIOUS DISEASES.

DR. J. D. ROLLESTON has brought out a second edition of his "Acute Infectious Diseases: A Handbook for Practitioners and Students."[1] The faults of the earlier edition which appeared five years ago, are repeated and nothing short of complete rewriting will make the book suitable for either class of reader. When an author sets out to deal fully with all the commoner infectious diseases in four hundred pages, he has no space to waste. A bibliography is out of place in a work of this size and it is bad enough to find that nearly thirty pages are occupied by lists of references to various authors, good, bad and indifferent. Not one student or practitioner in a hundred will trouble to look up a single one of these references. But in the text itself we find the evil carried to its limit. To choose one at random out of a host of examples, we find on page 387 a reference to E. Giraud of whom, we confess, we are ignorant. Tracing this to its source we read the following: "Giraud has recently collected from literature forty-four cases of recurrent smallpox which he divides into two groups. In the first, which consisted of five cases, a discrete first eruption was followed by an intense second attack, which in three instances was fatal. In the second group a typical first eruption was followed by a milder attack. In eight cases a third and still milder attack ensued, and in two instances there were four or five successive eruptions."

Now all this may be true or it may not. Neither M. Giraud nor anyone else can aver or deny it. The point is that there is no room for such rubbish in a book of this kind.

Following eight pages on the pathology and symptoms of the diphtheritic paralyses, finely written and full of interest, we look eagerly to the next subject, the pathology *et cetera* of the cardio-vascular system. We find that all that can be said about it is confined within a page and a half and to our dismay we find that much of this consists of "rubbish" of the kind indicated above. The most important feature of diphtheria is dismissed in a few words, yet there is plenty of room to describe at length nervous lesions in scarlet fever, diphtheritic hemiplegia, *erythema infectiosum* and so on.

Dr. Rolleston's wide reading has been his undoing. We again beg him, when a fresh edition is called for, to scrap the present volume in its entirety and to give us out of his vast experience and knowledge more information on subjects about which we really do want to hear.

[1] "The Essentials of Chemical Physiology for the Use of Students," by W. D. Halliburton, M.D., LL.D., F.R.S., J. A. Hewitt, Ph.D., D.Sc., and W. Robson, Ph.D, D.Sc.; Twelfth Edition; 1929. London: Longmans, Green and Company. Demy 8vo., pp. 394, with illustrations. Price: 9s. net.

[2] "Surgery in the Tropics," by Sir Frank Powell Connor, D.S.O., F.R.C.S., D.T.M. & H.; 1929. London: J. and A. Churchill. Post 8vo., pp. 301, with illustrations. Price: 12s. 6d. net.

[1] "Acute Infectious Diseases: A Handbook for Practitioners and Students," by J. D. Rolleston, M.A., M.D. (Oxon), M.R.C.P. (London), F.S.A.; Second Edition, Revised and Enlarged; 1929. London: William Heinemann (Medical Books) Limited. Demy 8vo., pp. 427. Price: 15s. net.

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The Lead Problem in Queensland.

For a period of about thirty-eight years it has been recognized that lead poisoning among children is commoner in Queensland than in any other part of Australia and perhaps in any other part of the world. The manifestations throughout the whole of this long period have been evident. Wrist drop and foot drop, colic, neuroretinitis and ocular palsies were recognized without difficulty and without doubt as the result of lead absorption and intoxication. In 1904 Dr. J. Lockhart Gibson with extraordinary perspicacity and pertinacity traced the source of the lead to the powder of the scorched paint on the wooden railings of verandas. He set up the thesis that children living in hot Queensland, spent much time on these guarded verandas, fingered the erstwhile painted railings, picked up a quantity of the powder under their nails and sucked their fingers. The chain of evidence seemed to be complete and Dr. Lockhart Gibson's achievement gains still further in importance by the ancillary evidence that he procured and published. He demonstrated that if the patients with ocular signs were treated in an early stage by lumbar puncture, removal from the veranda, the exhibition of sodium sulphate and sulphuric acid and later of iodide of potash, the palsy and the neuritis could be rapidly and completely cured. He further showed that the urine and fæces of the children suffering from the various forms of saturnism contained minute quantities of lead.

Despite the thoroughness of his work, there were, however, certain points which were difficult to explain. The quantity of lead recovered from the excretions was extremely small; no lead was found in the excretions of apparently healthy children exposed to the paint powder on the verandas; a soluble carbonate of lead, if swallowed, would be converted into the insoluble chloride in the stomach and would thus tend to escape absorption, particularly if the ingestion occurred of very small quantities spread over a long period. It was obvious to us about the year 1917 that more exact biochemical information was needed. A somewhat unfortunate controversy took place in 1922 after Dr. S. A. Smith had given evidence before the New South Wales Board of Trade on lead poisoning. The medical profession in Queensland, convinced that Dr. Lockhart Gibson has proved his case, demands the prohibition of the use of paints containing lead for outside woodwork. The trade, including the manufacturers of paints and the users of paints, that is the painters, resist this demand. The legislature seems to be relatively indifferent. It is quite obvious that if it can be proven beyond reasonable doubt that dried and powdered lead paint is actually a source of lead poisoning in children, adequate protection must be afforded to the people by the legislature.

There are certain facts that are sufficiently definite to be used as a starting point in any inquiry. Apart from the clinical experience of Dr. Lockhart Gibson and many others dating back as far as 1892, of an undue incidence of plumbism with paralytic and ocular signs, Dr. D. Gifford Croll and Dr. L. J. J. Nye have recently called attention to the excessive mortality from nephritis in young people. The mortality from acute nephritis is higher in Queensland than in any other State of Australia. This holds good for all age groups, but it is particularly striking during the third and fourth decades. The mortality from chronic nephritis in the first, second, third and fourth decades is much higher in Queensland than in any other State. In the third decade it is over five times that of the next highest rate. It is quite obvious that Dr. Croll's contention that there is some factor at work in Queensland which does not operate in other States, is correct. Dr. Nye has carried out an investigation into the circumstances of eighty patients treated either in hospital or in private practice during 1927 and 1928 for chronic nephritis. Of the eighty patients, forty-two stated that they

had not had any previous illness; fourteen stated that they had been treated for lead poisoning. No other single ætiological factor occurred more than five times in the series. If these histories can be accepted, it would appear that in 17·5% of Dr. Nye's patients lead was a possible causative agent in the production of chronic nephritis. Further inquiry disclosed the fact that of the remaining sixty-four patients twenty-two had been interviewed and questioned. Twenty stated that they had spent their childhood in wooden houses in Queensland on which the paint was dry. Sixteen of the patients had been nail-biters. He gives some other details of the possible relationship between the dried lead paint on the wooden railings and the subsequent nephritis. All this is very suggestive and is sufficient to justify a demand for a searching scientific investigation into the incidence of lead poisoning in Queensland, the sources of the lead, the effects of the intoxication, the immediate and remote mortality and the possibilities of preventing lead poisoning. Although it may be wise to maintain an open mind in regard to the question of the absorption of a soluble carbonate of lead through the gastro-intestinal tract and to a few other aspects of this rather complex matter, the circumstantial evidence is extremely strong in favour of a slow poisoning of children with lead in Queensland. The authorities cannot ignore the fact that the people of Queensland suffer from chronic nephritis much more frequently than do those of other States and that the death rate from this disease is excessive. They must also realize that plumbism is unduly prevalent among the children of the cities of the State and that a great deal of harm results.

A scientific working commission should be appointed without delay. A political commission would be useless, for the points at issue are those that cannot be answered by the taking of evidence or the cross questioning of patients or doctors. Experimental work is waiting to be carried out. The commission should determine the form of lead that is ingested or inhaled, the quantity that is absorbed, the manner in which the absorbed lead is stored and the method and rate of its excretion. The evidence of the source of the lead will have to be investigated with care, without bias or preconceived ideas. It is immaterial whether the State or the Commonwealth Government appoint the commission; it is material that a commission should be appointed at once, that its reference should be a wide one to enable it to investigate any problem connected with plumbism in Queensland and that the members of the commission should be persons competent to carry out scientific research.

Current Comment.

BLOOD REGENERATION.

THE power of the body to recover after injury or loss of tissue may be observed in many conditions. After loss of blood the same recuperative power is manifest. Nature's efforts to repair damage are not always recognized by the clinician. It is often forgotten that, even in hæmolytic anæmia, reparative processes take place and destroyed erythrocytes are largely replaced. If it were not so, death would occur much earlier than it does. The question is worthy of study, particularly as it affects different forms of anæmia. A great deal of work has been done on the subject and a lengthy review of the literature has recently been made by F. S. Robscheit-Robbins.[1]

This author contrasts anæmia resulting from hæmorrhage and hæmolytic anæmias. As long ago as 1911 Price Jones carried out an investigation in order to compare bone marrow and the blood changes in these two forms of anæmia. He used phenylhydrazin to destroy the red cells in rabbits. After injection of this drug he found changes resembling those seen in pernicious anæmia. He described these as a "metromegaloblastic bone marrow" and "megalocytic blood." Robscheit-Robbins states that Price Jones presumed that normal cell formation is thus partially inhibited and that this has to be reinforced by a production of metrocytes. He adds that the bone marrow gradually becomes depleted of very early forms, both metrocytes and megaloblasts. This is not a very clear way of explaining what happens. The bone marrow is depleted of early forms because they are hurried into the circulation to take the places of the cells which have been destroyed. If they were to be kept in the marrow until they became mature, the circulation would be inadequately provided with cells and the organism would cease to exist. Normal cell production is not inhibited, but interrupted. Robscheit-Robbins goes on to state that after removal of blood normal cell formation is not interfered with, but is stimulated and while it is supple-

[1] *Physiological Reviews*, October, 1929.

mented by the production of metrocytes, a large number of these cells remains in the bone marrow and becomes mature. Bone marrow which has been affected by hæmorrhage, has not been depleted to the same extent as that subjected to injury by phenylhydrazin. The changes which occur in the bone marrow in such a hæmolytic anæmia as pernicious anæmia, are of course well known. The increase in the amount of red marrow is the result of the attempt to supply cells in place of those destroyed. It must be recognized that the increased red colour of the marrow does not *per se* prove the existence of medullary hyperplasia. A similar red appearance may be produced in the marrow by congestion such as results from the application of a tourniquet or from cardiac decompensation and its subsequent circulatory changes.

Robscheit-Robbins refers to comparisons made by Itama and by Ritz into the rapidity of the regeneration following hæmorrhage and the production of hæmolytic anæmia by means of a drug. These observers found that repair from phenylhydrazin damage is more rapid than that following loss of blood by actual removal. Price Jones held that these observers were wrong in basing their conclusion on hæmoglobin value per unit of blood and not on any estimation of the total circulating hæmoglobin. In other words, it is necessary in these circumstances to determine the volume of the circulating blood. This may be done by the method of Haldane which depends on the fact that carbon monoxide, when inhaled, combines with hæmoglobin to form carbon monoxide hæmoglobin. There is also the simpler but less accurate method of Keith, Rowntree and Geraghty. In this method a non-diffusible dye is injected into the blood and its dilution is estimated. Robscheit-Robbins emphasizes the views of Price Jones in regard to blood volume and looks upon this as absolutely essential to the correct interpretation of any results dealing with regeneration. Price Jones pointed out that regeneration from phenylhydrazin injection may be arrested or masked for a period of six days and he postulated a direct toxic action of the blood on the bone marrow. Robscheit-Robbins points out that such a delay is not observed after loss of blood by hæmorrhage and that the colour index is not increased as it is in a hæmolytic anæmia. After a hæmorrhage the first thing which happens, is the restoration of blood volume. Pending this there is an adjustment by contraction of the smooth muscle in the vessel walls to the amount of fluid which they contain. The lost plasma is replaced by fluid of an identical composition from the connective tissue spaces of the body. The hæmatopoietic organs immediately take on an undaunted activity to replace the lost cells. On the other hand, when phenylhydrazin or some drug with a similar action, such as saponin, is injected, there is no alteration of blood volume; by the destruction of erythrocytes hæmoglobin is set free in the plasma, but there is no excess of metabolites. Regeneration will occur and the suggestion of Price Jones of a direct toxic action of the drug on the bone marrow is most reasonable. It would be very surprising if a drug, powerful enough to destroy blood corpuscles, had no direct action on the tissues, presumably at least as delicately constituted as the corpuscles themselves which give rise to the corpuscles. The fact that the hæmatopoietic tissues are not so accessible to circulating poisons as the red blood corpuscles is probably one factor in the discrimination. It would be reasonable to suppose that in primary aplastic anæmia characterized by absence of response in the bone marrow, the infective agent has either a greater affinity for or has easy access to the hæmatopoietic centres. Robscheit-Robbins quotes Bunting as having shown that bone marrow injury may be one of varying degree, dependent on the method of administration of the toxic agents as well as upon the amount introduced.

The relation of aplasia in the bone marrow to anæmia from hæmorrhage is of interest. Robscheit-Robbins states that Blumenthal and Morawitz raised the question whether bone marrow can be rendered aplastic by long sustained blood loss. These authors obtained results which were not conclusive. Robscheit-Robbins states that he and Whipple have accumulated evidence against this suggestion by the production of severe anæmia due to hæmorrhage constantly sustained and of three to four years' duration. The suggestion that the hæmatopoietic response might become exhausted is interesting, but it is contrary to the conception of an infective agent as the cause of aplasia of the marrow. If an aplastic anæmia occurred in an individual who was subject to repeated hæmorrhages, it would be right to assume the introduction of an infective agent. It is well to point out at this stage that the anæmia resulting from the use of a drug such as phenylhydrazin is not strictly comparable with that occurring in the body and due to an infective agent.

As far as the effect of phenylhydrazin on the erythrocytes is concerned, it has already been stated that it is reasonable to suppose that the drug will have some effect on the marrow. Although the hæmopoietic system of a person with *polycythæmia vera* is not comparable with that of a normal person, the action of phenylhydrazin on the blood of such a person may be referred to. It is illustrated in the report of a case by Dr. J. F. Chambers in The Medical Journal of Australia of March 30, 1929, at page 436. Dr. Chambers pointed out that the use of phenylhydrazin is attended by a leucoblastic reaction. This indicates an action of the drug on cells of the hæmatopoietic system generally as well as on the erythrocytes.

Merely the fringe of the subject has been touched upon in the foregoing. The chemistry of blood regeneration, for example, is of fundamental importance, especially in regard to the oxygen supply of the tissues. Elucidation of the part played by physical agents and of the action of animal tissues and metals in anæmia is likely to shed light on the process of blood regeneration. These must be left for future consideration.

Abstracts from Current Medical Literature.

MORBID ANATOMY.

Glomerular Nephritis.

Leone McGregor (*The American Journal of Pathology*, November, 1929) has made a microscopical study of tissue taken from the kidneys of sixty persons who died of acute and chronic glomerular nephritis. She gives a review of the literature and summarizes the accepted views. She then gives details of her own findings. It is generally held that there is a definite proliferation of glomerular endothelium in the acute stages of nephritis. While the leucocytic exudate has been described as polymorphonuclear, the origin of mononuclear cells within the capillaries is doubtful. Protoplasmic, albuminous and fibrinous types of intracapillary network have been reported, but there is no agreement on this point. It has been established that proliferation, degeneration and desquamation of glomerular epithelium are one part of the morphological change, but there is no uniform explanation of the origin and organization of the cells of the crescent. The changes in the *vas afferens* have been regarded for the most part as secondary to glomerular inflammation. But little attention has been directed towards alterations in the glomerular basement membrane and to hyalinization of glomeruli. The author finds that intracapillary cellular increase is chiefly endothelial and is explained by numerous mitoses. The leucocytes are polymorphonuclear and are much less numerous than the endothelial cells. A small amount of fibrin and *débris* is found in most of the capillaries. The extracapillary changes consist of proliferation, degeneration and desquamation of glomerular and capsular epithelium. They are easily distinguished from intracapillary lesions because the glomerular basement lies between. Crescent formation may be due to capsular epithelial proliferation or to a combination of capsular proliferation and glomerular epithelial desquamation. In the early stages hyaline fibres appear between the cells and soon become continuous with the capsular basement membrane. Hyaline fibres also appear inside the glomerular capillaries. They soon form a definite meshwork enclosing the intracapillary cells. This is the initial stage of hyalinization of the glomerulus. It takes place in all the glomeruli, but not always to the same degree. When every loop is occluded, the circulation cannot continue. There comes a stage when the glomerular loop consists of a few flattened epithelial cells, a basement membrane and a lumen completely filled with a hyaline mass enclosing a few nuclei. The end result is a sphere of fibrous connective tissue containing practically no nuclei. The origin and composition of the intracapillary hyaline fibres are undetermined. The finding of a glomerular cellular increase, usually of monocytes, following pneumonia and other infections is not to be confused with clinical nephritis.

Lipoid Nephrosis.

E. T. Bell (*The American Journal of Pathology*, November, 1929) has discussed the question of lipoid nephrosis. Nephrosis is defined as a degenerative disease in which the lesions are restricted chiefly to the tubules. All the clinical phenomena of lipoid nephrosis, namely, albuminuria, œdema, normal blood pressure, hypercholesterolæmia, decrease of the plasma protein with reversal of the albumin globulin ratio and normal blood nitrogen, may occur in a less pronounced form in glomerulonephritis. There are many transition forms between lipoid nephrosis and glomerulonephritis. These are a mixed type or nephritis with a nephrotic *Einschlag*. The author describes the histological appearances of ten large fatty kidneys with tubular atrophy, taken from persons who suffered clinically from nephritis. Four of these were classed as pure lipoid nephrosis, three as nephritis with nephrotic *Einschlag* and three as of uncertain type. Lipoid nephrosis is to be regarded as a form of glomerulonephritis in which the glomeruli are damaged, but their capillaries are only partially obstructed, so that they continue to function and tubular atrophy does not occur.

Primary Carcinoma of the Liver.

V. H. Moon (*Archives of Pathology*, December, 1929) has reported a case of primary carcinoma of the liver in which metastasis in bone occurred. The patient was a man, forty-five years of age, a negro, who suffered from spontaneous fracture of the neck of the right femur. The patient died nine weeks later after exploratory laparotomy had revealed a growth in the liver. On microscopical examination primary carcinoma of the liver cells was found, the carcinomatous masses distending the lumina of the portal veins. The neck of the femur at the site of the fracture consisted of metastasis from the liver growth. The author draws attention to the extreme rarity of bony metastasis with primary hepatic carcinoma. He was able to find records of only five cases in the literature.

The Pancreas in Non-Diabetic Persons.

Shields Warren (*Archives of Internal Medicine*, November, 1929) has reported on the condition of the pancreas found on *post mortem* examination of the pancreas of one hundred and fifty-six non-diabetic persons. The causes of death ranged from acute conditions such as enteric fever, pneumonia and post-operative pulmonary embolus to various chronic conditions; among these the late manifestations of carcinoma were frequent. The ages of the subjects varied from eight days to eighty-seven years. Practically any lesion found in the pancreas of diabetic patients can be duplicated in the pancreas of non-diabetic persons, though the occurrence of lesions of the islands of Langerhans is much less in the latter group. In 130 pancreases the islands were normal and 40 of these pancreases were the seat of interstitial pancreatitis. The lesions in the islands of the other pancreases included pyknosis, varying degrees of fibrosis, hyaline changes, hydropic degeneration, the appearance of mitotic figures, hæmorrhage and adenoma. Interstitial pancreatitis occurs too frequently in non-diabetic persons to be considered a lesion characteristic of diabetes. Lipomatosis is often related to the amount of body fat. It is impossible from a study of the pancreas to diagnose the presence or absence of diabetes.

Carcinoid Tumour of the Appendix.

H. Barth (*Virchow's Archiv für Pathologische Anatomie und Physiologie und für Klinische Medizin*, July, 1929) describes the occurrence of an extensive neuroma and of a small carcinoid tumour in the atrophied appendix of a woman, seventy years of age, who also suffered from pulmonary and laryngeal tuberculosis. The distal two-thirds of the appendix were occupied by an axial neuroma which was sharply differentiated from its surroundings. In the immediate neighbourhood of the nerve fibres in the submucosa were numerous epithelial cells containing silver-staining granules. In the distal part of the appendix these were so numerous that they displaced the neuroma and gave rise to the appearance of a definite tumour-like structure. The author also refers to the finding of syncytial giant cells in a carcinoid tumour which had produced metastases in the ovary. He refers to the fact that Obendorfer has found ganglion cells and similar syncytium in giant growth of the appendix with ganglio-neuromatosis. He believes that the giant cells are the progenitors of the carcinoid cells. He also states that carcinoid tumours may arise in a chronically inflamed as well as in an acutely inflamed appendix. Conversely through their situation carcinoid tumours may favour the occurrence of acute appendicitis.

Miliary Aneurysms of the Brain.

F. H. K. Green (*The Journal of Pathology and Bacteriology*, January, 1930) has examined the brains of ten persons who had suffered from arteriosclerosis. In three undoubted miliary aneurysms were found. One of these was a saccular or dissecting aneurysm and one was fusiform; it was impossible to classify the third from the few sections obtained. Each of the three arose from a grossly diseased parent trunk. Two of the aneurysms had ruptured and had given rise to small hæmorrhages in the brain substance. In the third thrombosis was complete and there was an associated zone of ischæmic softening. The author suggests that

miliary aneurysms arise only when atheroma involves the *tunica media* of an artery to an extreme degree. The process responsible for the production of saccular aneurysms is the stretching and rupture of the necrotic *intima* and *media* leading to effusion of blood into the Virchow-Robin space, followed by condensation and distension of the *adventitia*. The *adventitia* may undergo secondary rupture and so give free communication between the lumen of the parent artery and the surrounding tissues. In this way miliary aneurysms may be responsible for some cerebral hæmorrhages. Complete thrombosis of miliary aneurysms may give rise to foci of ischæmic softening in the brain.

MORPHOLOGY.

The Influence of Castration on the Involution of the Thymus.

JOLLY AND LIEURE (*Comptes Rendus des Séances et Mémoires de la Société de Biologie*, December 6, 1929) give results of experiments on guinea-pigs to show the influence of castration on the involution of the thymus. In this animal differentiation of the seminal tubules begins at about the fortieth day and spermatogenesis takes place at two and a half months, the testes being fully active at three months. The first indication of involution of the thymus appears at two and a half months and is almost always apparent at three months. Experiments were made on thirty-five male guinea-pigs with others as controls, all animals being of known age. The technique consisted of castration, usually between fifteen and thirty days, and the animals were killed when two and a half to six months of age. It is found that the weight of the thymus of the castrated is greater than that of the control animals; histological examination reveals a less degree of involution; this difference is plainly seen in animals killed at three to six months. It is usually less appreciable before three months, when involution is scarcely visible in the control. The difference is most pronounced at about four to five months and then less noticeable from five to six months, when the thymus of the castrated animal regresses and resembles that of the normal animal of the same age. Thus in the guinea-pig castration, performed before sexual maturity and especially whilst the seminiferous tubules are in the indifferent stage, has the effect of retarding involution of the thymus. These results confirm the work of Gellin on the rabbit.

The Parathyreoids in the Anura.

RESULTS of a histological examination of the parathyreoid glands of the American bull-frog, *Rana catesbeiana*, are published by R. A. Waggener (*Journal of Morphology*, September 5, 1929). The parathyreoids are four separate bodies, each with a connective tissue capsule surrounding a parenchyma of epithelioid cells forming the bulk of the gland. These cells are arranged in cords, densely massed. Beneath the capsule is a close capillary network sending vessels accompanied by fibrous trabeculæ from the capsule into the parenchymatous tissue. An interesting cyclic process occurs in the parathyreoids of *Rana catesbeiana*, differing in many respects from that of *Rana temporaria* described by Romeis. The gland cells gradually degenerate by vacuolization and liquefaction, accompanied by nuclear chromatolysis and pyknosis, finally resulting in liquefaction (in colloid form) of the parenchyma, except a single layer of cells beneath the capsule; the latter remains intact and distended by the colloid content. Regeneration of the parathyreoid which begins before cytolysis is complete, occurs from localized centres of growth in the remaining subcapsular parenchymatous layer; the growth centres which manifest frequent mitotic figures, are usually associated with blood vessels. The colloid which differs from that of the thyreoid gland, is slowly resorbed, whilst the epithelioid tissue assumes a cord-like arrangement and finally the compact condition described above. The author suggests that accessory parathyreoids arise secondarily during seasonal regeneration rather than primarily from other gill pouches. Degeneration does not occur simultaneously in all four glands of the animal. A cycle of parathyreoid activity apparently occurs in all individuals of this species during late winter and early spring, doubtless correlated with seasonal changes in other glandular organs.

The Postnatal Growth of the Cornea and Palpebral Fissure.

CHARLES HYMES records a series of studies made upon the growth of the cornea in nurses, medical students, school children, children of pre-school age and new-born infants (*Journal of Comparative Neurology*, October 15, 1929). Briefly, the average horizontal corneal diameter of the new-born child, whether male or female, was found to be 9·9 millimetres. Practically all of the postnatal growth of the cornea takes place during the first half year of life and it usually reaches its adult diameter, 11·8 millimetres, between six and twelve months after birth. Thus it will be seen that it differs from the general course of postnatal growth of the eyeball as a whole. The latter is characterized by a rapid increase in infancy and early childhood followed by a slower growth until maturity. On the other hand, the growth of the lid fissure is not so rapid in the first year as that of the cornea, but it continues at a slow rate until general body growth ceases. No significant sex difference was found in the absolute diameter of the male and female cornea. The palpebral fissure grows rapidly during the first two years of postnatal life and much more slowly thereafter. By the fifteenth or sixteenth year it is near the average adult size of 29·7 millimetres. The average projection of the eyeball for both male and female new-born infants is 5·84 millimetres. It tends to increase with great rapidity in the first year, then more slowly until the thirteenth year and finally still more slowly up to twenty-two years of age. The average projection in young adults is approximately 15 millimetres. This projection is measured from the lateral margin of the orbit to the apex of the cornea. The instrument used was a Hertel reflecting exophthalmometer. A series of curves and tables giving the data which have been measured in graphic form, is included in this paper.

The Nerves of Dura Mater.

N. DOWGJALLO (*Zeitschrift für Anatomie und Entwicklungsgeschichte*, June, 1929) has carefully examined the nerves of *dura mater*, especially in man. He remarks that such an examination presents many difficulties, especially in the bridging over between macroscopical and microscopical observations. In his mammalian material he washed out the blood vessels of the chloroformed animals and then injected a neutral red-methylene blue stain and fixed it by means of Kondratjew's fixator. Naturally great difficulty was experienced in examining human material, but fairly satisfactory preparations were obtained from new-born children which had died at birth. The author briefly reviews the literature which extends back to Valsalva's time, though Arnold in 1831 seems to have given the clearest account among the early observers. He then examines the innervation in the region of the middle cranial fossa. In the dog and cat he finds in this situation three groups of nerves, an anterior, a middle and a posterior. In man the main rôle in the innervation is played by the middle group. In one of his figures he shows a branch arising from a network of thin fibres, lying between the second and third branches of the Gasserian ganglion. This branch joins with the *nervus spinosus* of Luschka and forms an anastomosing network accompanying the middle meningeal, the fine branches ultimately reaching with the vessels to the sagittal sinus. The hinder branches found in mammals are also found in man, but are short and branched to the *dura mater* in the immediate neighbourhood of the Gasserian ganglion. Their origin lies in the ophthalmic division or in a network bound up with it. In the anterior fossa the nerves run in correspondence with the vessels. The nerves of the *tentorium cerebelli* and of the *falx cerebri* are also described, a whole series supplying the *tentorium* apart from the main Arnold's nerve, while the *falx cerebri* derives its supply from the nerve of the anterior fossa, from the middle meningeal nerve network and from the nerve of the *tentorium*. The author also discusses fully the relationship of these nerves to the nerves of the blood vessels.

British Medical Association News.

SCIENTIFIC.

A meeting of the Victorian Branch of the British Medical Association was held at the Ballarat District Hospital, Ballarat, on October 12, 1929, Dr. B. T. Zwar, the President, in the chair.

Mistakes in Practice.

Dr. Ian McNeil read a paper entitled: "Mistakes I Have Made in Practice." This paper was published in the issue of December 28, 1929, at page 911.

Tarsorrhaphy.

Dr. J. C. Douglas read a paper on tarsorrhaphy.

Kienboch's Disease.

Dr. J. C. Best showed a man, aged twenty-one years, a carpenter, who had complained of swelling and pain in the right wrist joint of four months' duration. An X ray film revealed an area of rarefaction in the semilunar bone. The wrist had been put in a "cock-up splint" for five weeks without much improvement. The patient had been forced to change his occupation. Dr. Best considered the condition to be typical of Kienboch's disease which was a type of osteochondritis. He said that the pathology was vague and surgical authorities were not agreed as to the best treatment.

Dr. Victor Hurley said that little was known of the pathology of this form of bone dystrophy. It was probably allied to Köhler's disease of the tarsal scaphoid bone and to Perthes's disease of the hip joint and possibly to Calvé's disease of the vertebral bodies. It was nearly always seen in young adults of about the age of Dr. Best's patient and was usually ushered in by a period of pain and swelling and signs of a low grade arthritis. These symptoms tended to subside for a few weeks or months and to recur at intervals.

The treatment had not been standardized, but the most satisfactory method was to treat the condition as if it were a mild arthritis. The local lesion improved more rapidly if the part were immobilized than on active movements, diathermy *et cetera*. The X ray appearances seemed to be permanent even after clinical cure.

Dr. A. E. Coates pointed out that the semilunar bone of the carpus was the keystone of an arch. In the patient under discussion a thrust on the middle metacarpal produced pain. Such a thrust was transmitted to the capitate bone which articulated on its proximal surface with three bones. The middle of these was the semilunar or lunate, which tended to take the weight of the thrust, and this was probably the reason why it was picked out in this type of dystrophy.

Malignant Disease of the Male Breast.

Dr. W. J. Rawlings showed a man, aged sixty-five years, who had noticed bleeding at the nipple of the left breast twelve months previously. This had continued intermittently ever since with a small scab forming and gradual growth around the nipple area.

On examination there was a fungating growth five centimetres (two inches) in diameter around the nipple area of the left breast. It was hard, with everted edges and firmly attached to the *pectoralis major* muscle and incorporated in the skin. Several glands were palpable in the axilla; one was large. They were hard, but not tender.

Dr. B. T. Zwar said that carcinoma of the male breast was a comparatively rare disease, representing one in every hundred cases of breast cancer. In a recent review of an inquiry into cancer of the breast conducted under the direction of Sir George Newman, of the Ministry of Health in England, the results did not indicate any greater virulency as a direct cause of death in young people as compared with older people, but emphasized the importance of treatment before metastases had occurred. With such early treatment the records revealed 70% of cures after an interval of ten years compared with only 20% of cures in cases in which metastases had occurred before operation.

Dr. Zwar pointed out that metastases occurred along the larger lymphatics by embolic spread and the tumour should be handled as little and as gently as possible to avoid pressing malignant cells into the lymphatic circulation. It was possible that metastases were formed relatively early in cases of cancer of the breast owing to the free movement of that organ.

In his opinion, if a patient were seen early, the best method was to remove it with the knife. There was no way of being certain whether an apparent cure by radium was real or permanent owing to the possibility of living cancer cells having been occluded in fibrous tissue following the local reaction.

Dr. Victor Hurley said that he had never seen malignant disease in the male breast which had been operable at the time of observation. Adhesions to the pectoral muscles and involvement of the axillary lymphatic glands occurred very early. In the present patient both the axillary and the supraclavicular glands were palpably enlarged and he did not consider that the patient was suitable for operation.

Pernicious Anæmia.

Dr. Rawlings also showed a male patient, aged sixty-seven years, who had been quite well until about two years previously. He had been a strong man and an engineer in Malay and Siam for twenty-five years, during which time he had had malaria many times. The first attack had occurred in 1907, then an attack had occurred about every two to three years till last attack in 1926. The patient had had a very severe carbuncle four years previously and enteric fever when he was nineteen or twenty years old. He had worked in mines in Ballarat and the Malay States. About two years previously he had begun to feel off colour while in Malay; he had felt as if some sickness was coming on. He had suffered from slight lethargy and listlessness, had not been inclined to go on long trips, as he felt he might have become ill while away. He had picked at food and had not cared for a favourite dish, curry; he just did not feel inclined for it. He had noticed slight dyspnœa, especially if he had to walk up a hill, but could still walk twenty miles a day without excessive fatigue. He had had a daily action of his bowels. He had been advised to take a holiday from the tropics.

He had come to Australia about November, 1927, and was picking up slightly. He had eaten much green food, salads *et cetera* which he had relished till he gradually lost appetite for them; he had also lost appetite for meat and bread and was still in the same condition. He had had some looseness of the bowels with urgency of action. He had gone to Melbourne Hospital about November or December, 1927, for six weeks as an out-patient. He had been given a barium meal which revealed no abnormality. He had still got no relief, had lost weight from 100·8 kilograms (sixteen stone) to 6·3 kilograms (ten stone) with loss of energy and anorexia. He had lived on a plate of porridge night and morning, this being all that he felt inclined to eat. No other symptoms had been present. He had consulted a gastric specialist, had had a barium meal and had had blood taken from his arm for a test. He had also had a fractional test meal. He had sought advice from Chinese, with neither good nor bad result.

He had attended the medical out-patient department at the Ballarat Hospital on December 20, 1928. Some looseness of the bowels had been present and on examination his condition had been similar to that found at the time of the meeting. A barium enema had revealed no abnormality. The erythrocytes had numbered 2,500,000 and the leucocytes 8,000 per cubic millimetre. No report of a differential blood count had been received. He had been regarded as suffering from either carcinoma of the colon, tropical dysentery or pernicious anæmia.

He had next been seen on March 30, 1929, and admitted to a medical ward. He had then stated that he had never had constipation, but still had about four motions per day, passing a soft formed stool, rather light in colour. He had been taking only a soft diet and had never noticed anything unusual about the motion.

On April 8, 1929, a barium enema had again been given and ballooning of the rectum had been noted with signs of obstruction at the sigmoid and an acute angle of large bowel also near the caecum. A barium meal at this time had revealed a peculiar twisting of the colon on carefully following the meal through, but no obstruction had been visualized and no stasis. He had been discharged on May 9, 1929, with a diagnosis of either chronic volvulus of the colon or anæmia of unknown origin. The blood had not reacted to the Wassermann test.

He had attended the medical out-patient department for a while and had been next seen and admitted on August 5, 1929. He had complained of pain in the right side of the chest, worse on taking a deep breath. At this time he had been much shorter of breath, much weaker on exertion, his bowels had again become loose when at home, he had vomited several times a day before admission and had had a sore tongue along the edges for the last two weeks. Anorexia and peckishness had still been present.

Examination had revealed a very sallow, pale man with a very dry inelastic skin. His tongue had been clean and moist, not red or glazed. His breath had been good. Examination of the radial pulse had revealed some arteriosclerosis; the pulse had been regular and of good volume and tension. The pupils had reacted readily to light and accommodation. The chest had been emphysematous with poor air entry and a moderately good note. At that time few râles had been audible at the right base with a friction rub. The chest was clear at the time of the meeting. The cardiac apex beat had been diffuse and not palpable, situated about the fifth intercostal space, 9·3 centimetres (three and three-quarter inches) from the middle line. The sounds had been poor in quality, but clear. The skin of the abdomen had been lax and dry as if the patient had lost weight. The liver, kidneys and spleen had not been palpable. No masses had been palpable. On rectal examination the prostate had appeared slightly enlarged; some ballooning of the rectum had been present. The systolic blood pressure had been 140 millimetres of mercury. The fundi had been normal.

On August 8, 1929, the erythrocytes had numbered 2,000,000 per cubic millimetre and the hæmoglobin value had been 70%. No nucleated red cells had been seen. Large red cells had been present. The tongue had still been sore. The patient had been put on to hydrochloric acid and liver.

On August 13, 1929, he had felt much improved; the erythrocytes had numbered 1,820,000 per cubic millimetre and the leucocytes 10,000, the hæmoglobin value had been 80% and the colour index 2. The film had been clear and some macrocytes had been found.

On August 28, 1929, the figures of the blood count had been 1,840,000, 12,500, 80% and 2 and "Karna Vita" had been ordered. On September 12, 1929, the figures had been 1,975,000, 10,000, 70% and 1·7. Several normoblasts and a few transitional myelocytes had been seen. On September 23, 1929, the figures had been 2,118,750, 10,000, 75% and 1·7. The erythrocytes had been more normal in size, shape and staining, no nucleated red cells had been seen; the leucocytes had been normal. On October 2, 1929, the figures had been 2,400,000, 10,000, 80% and 1·6. The differential count had been: Polynuclear cells, 66%; eosinophile cells, 2%; basophile cells, 0·5%; small lymphocytes, 22%; large lymphocytes, 2%; mononuclear cells, 2·5%; myelocytes, 7%; monocytes, 0·5%. No nucleated red cells had been seen, but many macrocytes.

On October 11, 1929, the figures of the blood count had been 2,800,000, 10,000, 70% and 1·3. Many myelocytes and premyelocytes had been present and two eosinophile cells with some macrocytes. The figures obtained by the urea concentration test had been 1·3% and 1·5%.

Dr. Rawlings said that he considered this an interesting case from the view point of diagnosis. Briefly there were gradual onset of anorexia and wasting, listlessness and some lethargy. Looseness of bowel had occurred with some lightness in colour of the stool; but the patient had been on a soft carbohydrate diet. The stools were fairly bulky. Pallor and definite anæmia were associated with disturbances of the circulation and of the oxygenating powers of the blood.

In the differential diagnosis several conditions had to be considered. Carcinoma of the bowel, colon or stomach had been excluded by repeated X ray examinations. In regard to tropical diseases and bowel upsets, malaria might set up malarial cachexia with secondary anæmia of erythrocytes to 2,000,000 per cubic millimetre, but in these circumstances there was usually a low hæmoglobin content and a low colour index with associated leucopenia and enlarged spleen (Tidy). *Ankylostoma duodenale* caused anæmia of a secondary type which might pass on to the pernicious type (Price), but the colour index was usually about one and there was an associated eosinophilia of 18·20%. Both of these were absent and associated with normal findings on examination of the fæces. There was wasting which was not usually present. In sprue stomatitis with subsequent atrophy was not present till late. Wasting and dyspepsia occurred with anæmia which in later stages might be indistinguishable from pernicious anæmia, but profuse frothy diarrhœa was absent from the history and diarrhœa had not commenced until the patient's return to Australia. In favour of chronic nephritis and arteriosclerosis were the pallor and some œdema of the feet and the low urea concentration of 1·3% and 1·5%. There was associated secondary anæmia, but in the terminal anæmia of chronic nephritis the hæmoglobin value was an index in inverse ratio of the creatinine content of the blood. In the patient under consideration the hæmoglobin value was remaining consistently high, so they were left with a diagnosis of secondary anæmia, leuchæmia or primary anæmia.

Dr. Rawlings said that he could not discover a primary cause for a secondary anæmia. Leuchæmias might be considered in view of the differential count, but the patient's condition did not conform to types as he was acquainted with them and there was the absence of an enlarged palpable spleen. Primary anæmia looked probable. There were the history with the above associated newly developed glossitis; the consistently low red count; the high hæmoglobin content; the high colour index, well over one, reaching two at times with films in which were macrocytes, red cells showing poikilocytosis and anicytosis; at one examination the presence of normoblasts, not again discovered; the slow but evident improvement with hydrochloric acid and liver diet. These pointed very conclusively, he thought, to pernicious anæmia, except for the disquieting differential count.

DR. S. O. COWEN said that he would not care to make a diagnosis without a more careful examination of the blood films. The condition appeared to be an anæmia of the pernicious type, either pernicious anæmia or something closely simulating it. Repeated X ray examinations should be made to exclude malignant disease of the alimentary tract. Of the tropical diseases sprue was the most probable, but the sore tongue had not been complained of as early as was usual in sprue. In the latter disease there was often a blood picture of anæmia of the pernicious type. Also consistent with sprue was the improvement on liver feeding. This had not been so rapid as was usual in pernicious anæmia. Taking all the available evidence into consideration Dr. Cowen thought that the condition was one of sprue of atypical mild chronic type.

DR. LESLIE HURLEY thought that there was not sufficient constructive evidence to make a definite diagnosis. It was not necessarily easy to find a cause for anæmia of the secondary type. Sometimes in such cases no cause for the anæmia was ever found. Any type of infection which could cause anæmia of the secondary type, could cause anæmia of the pernicious type. The important point in the present case was that the patient had a macrocytic anæmia and in most anæmias of this type the therapeutic response to liver feeding was good.

DR. T. E. GREEN said that as the condition presented all the classical features of pernicious anæmia, it should be placed in this category.

DR. J. JONA suggested that the condition might be due to chronic poisoning by tin or one of the other metals due to his occupation of mining and he considered the possibility worthy of thorough investigation.

DR. J. F. WILKINSON said that he had seen this patient two years before in consultation with Dr. J. Bell and he

thought that they had found that hydrochloric acid was absent from the gastric secretion. Dr. Wilkinson considered that pernicious anæmia was a clinical entity of unknown origin, that was to say, an anæmia secondary to some cause at present unknown.

The most important sign was the increasing size of the red corpuscles and this might not be recognized in an ordinary blood film examination.

The presence of abnormally large red corpuscles made possible a diagnosis of a condition of prepernicious anæmia and suitable treatment might prevent the development of the latter condition. This fact also pointed to the importance of the routine examination of the gastric contents in doubtful cases. The finding of a sore tongue and absence of hydrochloric acid should lead to an examination of a blood film for macrocytosis and poikilocytosis. Dr. Wilkinson had never seen a case of pernicious anæmia in which hydrochloric acid was present in the gastric contents, and this state might precede the development of pernicious anæmia by as much as ten years.

It was not wise to diagnose a condition as one of pernicious anæmia from the appearances of the blood film alone. It was more correct to speak of it as an anæmia of pernicious type and proceed to search for some possible primary cause, such as ankylostomiasis *et cetera*. The peculiar colour of the skin was an important sign in the recognition of pernicious anæmia and in the present case he considered that further test meals should be given after a stomach wash-out to test for free hydrochloric acid by Gunzberg's test.

The question of metal poisoning was an important one, but on the whole Dr. Wilkinson thought that Dr. Cowen's diagnosis of sprue was most probably correct. To illustrate the occurrence of occupational metal poisoning Dr. Wilkinson quoted the case of supposed radium poisoning of some girls who had been employed in painting the luminous figures on watches and who had suffered from a severe and progressive anæmia which was expected to be fatal. They had been given substantial compensation. The cases had been reported in the *Journal of the American Medical Association*, but a later report indicated that their illness might have been due to one of the other radioactive metals and that there was some hope of their recovery.

Dr. J. O'Sullivan said that in all cases of anæmia of unknown origin a cholecystogram should be taken as gall bladder infection was a not uncommon cause of anæmia. Opaque meal examination of the stomach might be of some value in these cases, as the rugæ of the gastric mucosa were flattened out in pernicious anæmia and also in the precancerous stage of gastric malignant disease.

Dr. W. T. Greening pointed out that the low urea concentration of 1·3 and 1·5 was consistent with advanced arteriosclerotic kidney changes and a large number of the patient's symptoms could be explained by chronic nephritis.

Capillary Nævus.

Acting on behalf of Dr. A. Guymer, Dr. Rawlings showed a baby, aged two and a half months, who was born with a port wine discoloration of the skin over the left parotid region. Two weeks after birth swelling had been noticed at the angle of the jaw and this had gradually enlarged. The swelling was usually soft and fluctuant, but on a hot day or occasionally after a hot bath it became hard. No difference in size had been noticed before or after feeds. One week previously the right side of the jaw had begun to enlarge. The condition had been similar to that on the left side.

On examination there were soft diffuse bilateral swellings at the angle of both jaws. The swellings were sharply limited, they could be pressed flat and refilled. The swellings were not continuous with the parotid glands which could be felt beneath. The buccal openings of the parotid glands were present and appeared to be active.

Dr. M. R. Healy considered the condition to be a capillary nævus with an underlying angioma. He recommended radium therapy.

Dr. A. P. Derham agreed with Dr. Healy's diagnosis and remarked that neither the course nor the consistency of the swellings suggested a sarcoma and they were rather more highly placed than the usual site of thyreoglossal cysts which were outgrowths from the developmental branchial clefts and somewhat resembled the present tumours in consistency.

Traumatic Psychoneurosis.

Dr. E. Sandner showed a male patient, aged sixty years, who had jarred his back carrying timber off a wharf thirty-five years previously. He had jumped down about two feet with one hundredweight on his shoulder. He had felt very weak afterwards and had noticed pain immediately; the pain had been severe for about half an hour and had then got easier. About two days afterwards he had complained of very severe headache. He had not had sore throat or cold. Next day he had taken a dose of oil and had then felt very weak, but had not gone to bed; the headache had persisted. About 4 p.m. he had walked down steps and his legs had "left him" and he fell to the ground. He had not had pain, but had felt weak. Then he had got up and walked into a room, had come out and had had a cup of tea but could not eat anything; he had then gone on to the veranda and his legs had again "left him"; he could not get up. He had been taken to hospital for five months. When he went to hospital he had had "severe pain all through system" and had been unable to move his legs at all. He had only just been able to move his right arm, the face had not been affected. After two days the power had come back to his arm. He had had retention and it had been necessary to catheterize his bladder once. He had then been able to pass his urine with difficulty. No incontinence had occurred, but difficulty in starting micturition. Once it was started, he was right. He had then lain for months; headache had improved and he had "sweated away to nothing." Then hot foments had been applied to the back. The kidneys had been very bad with much sediment in the urine when hot foments were applied to the back. After some months he had scarcely been able to move his legs, but had got some power in his body and could roll about to see his friends on the veranda, but could not walk. He had then tried hot sea baths for six months. His general condition had improved and he had then tried to walk by holding on to a rail, but could not bear any weight on his legs. He had gone back to Normanton Hospital. No improvement had resulted, so he had been sent to Brisbane Hospital. Batteries and massage had been applied and after a few months he had just been able to walk. It had been about two years before he walked. The patient's condition had remained the same until five and a half months before the meeting. He had felt weak, his legs had gone down and he could not rise. He had been quite conscious and had experienced terrible pains in the legs. Sharp shooting pains had been present on the outer side of both legs from the hip right down. He had felt pains only at night; they had recurred at times at intervals of two to three days. He had complained of terrible twitching down the legs and in the shoulders on and off until his arrival at Ballarat; the twitching was not so severe. He had had no difficulty with fæces or urine at any time and no cough. He had vomited occasionally in the morning before breakfast, particularly in summer time. Indigestion had been bad at times (about six to twelve attacks a year); an attack lasted a quarter of an hour to twenty minutes. During an attack there was very severe burning pain across the epigastrium, relieved by vomiting; sometimes it woke him at night between twelve and one o'clock. Appetite, previously very bad, had improved. Sleep had been good; prior to this he had been a poor sleeper, complaining of restlessness. He had been unable to walk or stand since falling five and a half months before. He had then been unable to move his legs.

Dr. Sandner said that after the above history was taken, the patient had been able to flex his knees by lying on his side in bed. The pupils had reacted to light and accommodation. The tongue had been clean, the breath good and teeth moderately good. The apex beat had been in the fifth intercostal space, 8·75 centimetres (three and a half inches) from the mid-line. The sounds had been clear. No abnormality had been detected in lungs or abdomen.

The cranial nerves had been normal. Sensation had been normal, except for inaccuracy in appreciation of heat

and cold on the lateral and posterior aspects of the left leg and the posterior aspect of the right leg. Slight loss of power had been noted in the left arm; the patient was naturally right handed.

Before the history was taken the patient had not been able to move his legs. The next day, when examination of the central nervous system was carried out, he could draw up his feet by lying on his side and move the toes of the left foot with the legs extended, but not the toes of the right foot. The wasting of both legs had been extreme, as shown by the following measurements: Above the knee joint on the left side 25 centimetres (ten inches), on the right side 22·5 centimetres (nine inches); at the level of the knee joint 33·75 centimetres (thirteen and a half inches) on the left side, 32·5 centimetres (thirteen inches) on the right side; below the knee joint 22·5 centimetres (nine inches) on both sides; above the ankle joint 16·8 centimetres (six and three-quarter inches) on the left side and 15·6 centimetres (six and a quarter inches) on the right side. Foot drop had been present in the right foot.

The triceps and biceps jerks had been equal and active, the knee jerks had been present, the left ankle jerk had been present and the right absent, the plantar reflex had been flexor in type, the superficial abdominal reflexes had been equal and active, the cremasteric reflexes had been equal and active, the deep abdominal reflexes had been equal and active.

The systolic blood pressure had been 180 and the diastolic pressure 100 millimetres of mercury.

Treatment had consisted in the administration of iodide of potash in doses of 0·6 gramme (ten grains) three times a day and in the use of massage, movement and stimulation.

On May 20, 1929, the patient had been able to lift his legs off the bed when lying on his side.

On May 31, 1929, he had felt well and had been able to sit on the side of the bed and swing his legs.

On June 5, 1929, he had sat on the side of the bed trying to push a small sandbag along with his feet, to lift a weight fastened to his foot and to kick a weight off his foot.

On June 10, 1929, he had been able to walk by holding on to the bed.

On June 12, 1929, he had been able to walk by steadying himself against the wall.

On June 16, 1929, he had been able to cross between two beds without support. For walking round the ward he had needed a small metal rod for balance.

On June 28, 1929, the patient had been able to walk moderately far without a stick. During his stay in hospital his temperature had not risen above normal and his pulse rate had varied between 68 and 88 in the minute. He had then been discharged to the out-patient department.

While he was in hospital, a number of special investigations had been carried out. On lumbar puncture clear fluid under normal pressure had been obtained. Neither the blood nor the cerebro-spinal fluid had reacted to the Wassermann test. No other abnormality had been discovered on X ray examination of the spine or pelvis. All the muscles had reacted to faradism. The *fundi oculorum* had apparently been normal. The figure obtained on examination of the second hour specimen in the urea concentration test had been 2·1%.

On October 7, 1929, a further examination had been carried out. No abnormality had been detected in the cranial nerve. The pupils had reacted to light and accommodation. On examination of sensation with pin prick, cotton wool, deep pressure there had been no loss and the patient had been accurate in his statements. The response had also been normal in regard to localization, with vibration and with heat and cold. The right arm had been slightly stronger than the left and the left leg more powerful than the right. On examination of the circumference of the lower limb the following measurements had been obtained: Above the knee joint 26·25 centimetres (ten and a half inches) on the right side, 30 centimetres (twelve inches) on the left; at the level of the knee joint 32·5 centimetres (thirteen inches) on the right side, 35 centimetres (fourteen inches) on the left; below the knee joint 22·5 centimetres (nine inches) on the right side, 25 centimetres (ten inches) on the left side; above the ankle joint 16·25 centimetres (six and a half inches) on the right side, 18·1 centimetres (seven and a quarter inches) on the left. A slight but definite movement of the big toe had been found on the right side. There had been no tremor. The triceps jerk, the biceps jerk and the supinator jerk had been slightly more active on the left side than on the right. The knee jerk and the ankle jerk had been absent on reinforcement. The plantar reflex had been flexor in type; there had been no knee clonus or ankle clonus. The superficial and deep abdominal reflexes had been equal and active. The cremasteric reflex had been present. Dysdiadokokinesia had been absent. Neither past pointing nor nystagmus had been present. The left knee joint had been swollen and had contained some fluid, fluctuation had been elicited and there had been no patellar tap. Palpable crepitus had been found in both knees on movement. There had been no limitation of movement. The joint had been neither tender, red nor hot.

Dr. Sandner said that in offering a differential diagnosis several conditions could be excluded. Syringomyelia might be excluded because of the absence of any dissociated anæsthesia, the recovery after initial loss and the absence of trophic disturbance after thirty-five years. Intracranial tumour was excluded because of the absence of any general signs of tumour, the length of time the disease had existed without getting progressively worse and the absence of signs of upper motor neurone paralysis. Tumour of the spinal cord was ruled out because of the absence of any definite sensory loss or progressive motor loss and the absence of upper motor neurone paralysis or involvement of sphincteric control. Pressure on the cord was not the cause because of no sensory loss in the saddle area, the sudden onset, the normal X ray findings, the absence of any loculation syndrome without progression of symptoms. Hæmatomyelia was excluded because of no upper motor neurone lesion and the sudden recurrence of symptoms with recovery of the full power of the wasted muscles. Extramedullary tumour was excluded because of the onset with involvement of arms and legs with almost complete recovery of the arms, the extent of the motor lesion with no evidence of a lower motor neurone lesion or sensory loss and the absence of objective sensory signs of root distribution.

Although they might suspect hæmorrhage as a cause because of the sudden onset and pain in the back, there was no evidence of any nerve root paralysis. Although the absence of a sudden onset might be explicable on the basis of a slow hæmorrhage, he thought this condition could be excluded on account of the absence of any sensory loss of root distribution with such a gross muscular wasting and the recurrence of complete paralysis of both legs with recovery.

Disseminated sclerosis could be excluded because of the absence of scanning speech, ankle clonus, ocular phenomena and increased deep reflexes.

Dr. Sandner thought that syphilis could be excluded because of the absence of response to the Wassermann test both in the blood and cerebro-spinal fluid and the absence of any other sign of syphilis. Neuritis could be excluded because of the absence of muscular tenderness, sensory symptoms or reaction of degeneration. Uræmia could be excluded because of the length of time the disease had existed and the result of the urea concentration test. The patient gave no history of any contact with lead. An old anterior poliomyelitis could be excluded because of the presence of deep reflexes, the recovery after the recurrence of complete loss of power.

This left a diagnosis of traumatic psychoneurosis. The swollen knee joint could be explained as a traumatic synovitis because the patient was using his legs more than ever since the original onset.

Dr. M. D. Silberberg congratulated Dr. Sandner on his able presentation of the case. Dr. Silberberg gave it as his impression that the condition was certainly not purely functional in origin. It seemed probable that there had been originally some hæmorrhages into the spinal cord, followed by long standing toxic myelitis, the infection possibly dating from catheterization.

DR. LESLIE HURLEY thought that there was a functional element added to the organic lesion. The only neurological sign of an organic lesion was absent right ankle jerk and as this was the only finding after a thirty years' course, he considered that hysteria constituted the chief element in the patient's illness.

LISTS OF MEMBERS.

THE lists of members of the several Branches of the British Medical Association in Australia are now in the press and will be available in a short time. Copies can be purchased from the office of THE MEDICAL JOURNAL OF AUSTRALIA at one shilling each.

Medical Societies.

CLINICAL SOCIETY OF THE HOSPITAL FOR SICK CHILDREN, BRISBANE.

A MEETING OF THE CLINICAL SOCIETY OF THE HOSPITAL FOR SICK CHILDREN, Brisbane, was held on October 24, 1929, Dr. G. P. Dixon in the chair.

Pituitary Infantilism.

DR. J. A. CAMERON called attention to a child, aged twelve years, who had been seen for the first time a week before the date of the meeting. She had had a dent in her head since birth. No medical practitioner had attended the mother at the confinement. The fact that the child had been undersized had not been noticed until she had reached the age of five years. She had grown very little since the age of seven years. There had been no increase in weight for some time, but her general appearance had improved. The mother had had four other children, all of whom were of normal size. The patient had suffered from severe frontal headaches and frequent vomiting. The vomiting had not always coincided with the headaches. There had been no headache for a month before admission. She had had no other illnesses. The child was in the fifth second class at school, but did not like school. She was said to be clever with the sewing machine. No examination of the blood had been carried out. There was excessive growth of hair on the arms. The urine contained neither albumin nor sugar. The child's weight at the time of admission had been 18·6 kilograms (forty-one pounds); the average weight for a girl of twelve years was given as 25·4 kilograms. Her height had been 129·5 centimetres (four feet three inches) as compared with the normal 198 centimetres. Her eyes had been examined by Dr. W. Lockhart Gibson; nothing had been found that would account for the headaches. An X ray examination had been carried out by Dr. B. L. W. Clarke who had reported that there was no definite evidence of a fracture of the skull. He had pointed out that at the base of the occiput a small portion of the bone appeared to be missing. The area was about 3·8 centimetres (one and a half inches) in length and was situated around the middle line. Dr. Clarke had formed the opinion that it was a congenital abnormality. The ossification around the base of the skull appeared to have advanced a little more than usual. The sutures of the skull had the appearance of having become united. Both the anterior and the posterior frontal sutures were closed. Dr. Clarke had further pointed out another interesting finding. There was an opaque area over the region of the lateral ventricle and a collection of opaque areas over the frontal and occipital bones of the skull. These shadows, in his opinion, indicated increased intracranial pressure which was giving rise to indentations on the inner table of the skull. The opaque area over the middle line of the skull when seen in lateral view was possibly the result of an increased amount of fluid in the third ventricle. The *sella turcica* appeared to be normal and the wings of the sphenoid also seemed to be normal. There was no definite abnormality seen in the anterior clinoid process, while the shadows of the maxillary and other nasal accessory sinuses were quite clear.

It was suggested that the epiphyses of all the long bones should be examined radiographically and if it were found that the epiphyses had ceased growing, there would be little doubt that the lesion was situated wholly in the pituitary body.

Bursa of the Semimembranosus.

DR. M. SHIRLEY LANE presented a child, aged seven years, with a swelling behind the left knee. Two years previously the child had had a lump at the back of the left leg with pain and stiffness in the leg and ankle in the morning. On examination a lump had been felt in the popliteal space, disappearing under the *semimembranosus* on extension. There had been no pain, redness or heat. The lump had been hard and knotted; no pulsation had been present. The child had had acute nephritis, but there had been no albumin in the urine for eighteen months, though the systolic blood pressure had been 132 millimetres of mercury. The diagnosis of a bursa under the tendon of the *semimembranosus* was made. Dr. Lane pointed out that this was an inflammatory condition and that these bursæ were easy to excise. They usually communicated with the joint, but the patients did well after excision of the bursæ.

Bronchitis and Bronchiectasis.

DR. GAVIN H. CAMERON showed a male patient, aged ten years, who had been admitted to hospital on October 17, 1929. He had attended as an out-patient in June, 1926, when he had been suffering from enuresis and a capricious appetite. At that time the child had been undernourished and anæmic. Examination of the fæces had been carried out for ova, but none had been found. There had been no basophilia and nothing abnormal had been discovered in the urine. In October, 1927, the child had been in hospital with pneumonia. In June, 1928, he had suffered from frequent colds, general ill health and enuresis. In July, 1928, he had been nervous and irritable and still had had enuresis. The mother had stated that he had attacks of sudden pallor, but that the child did not lose consciousness. Nothing abnormal had been detected on examination of the chest. In March, 1929, he had had sores and boils and "snuffles." He had been undernourished. A few pus cells had been found in the urine, but no other abnormal elements. There has been no reaction to the Wassermann test. The child had improved in May, but in June the cough had returned. In July the cold had improved, but there had been lassitude, lack of energy and absence of appetite. In August the child had coughed at night time. When admitted in October he had had a bad cold for two weeks and was very feverish. He had had no cold sweats. There had been loss of appetite.

On admission the child had looked ill. The tongue had been coated, but the throat had been normal. There had been dulness on percussion over the whole of the chest on the right side. Numerous moist sounds had been detected and the breath sounds had been somewhat harsh. A blood count had been undertaken. The red cells numbered 4,270,000 per cubic millimetre, with 85% hæmoglobin. The leucocytes had numbered 7,000 of which 60% had been neutrophile cells, 29% lymphocytes, 3·5% mononuclear cells and 7·5% eosinophile cells. Slight polychromasia had been detected. Two examinations of the sputum had been carried out, but no tubercle bacilli had been found. In the skiagram the lung shadow on the right side had been seen to be much increased; tuberculosis had been diagnosed.

Since admission the dulness on percussion had diminished. There were moist sounds on the right side at the base of the lung and a few rhonchi. The breath sounds were slightly diminished. At the time of the meeting there was still dulness at the right apex and over the upper part of the right lung, but the note over the lower lobe was the same on both sides.

Those present concluded that the condition was not tuberculous, but was probably bronchitis and bronchiectasis.

Acute Lead Poisoning.

DR. S. F. MCDONALD'S first patient was a female child, aged five years, who had been admitted on October 15, 1929, with the history that for one month she had not eaten her meals and had complained of nausea and pains in her abdomen. During the week prior to admission it had been noticed that the child was walking in a peculiar manner and she seemed to have no power in her right foot. She had complained occasionally of pains in her legs. There was a doubtful blue line on her gums. There was double wrist and foot drop. The red blood cell count was 2,390,000, the hæmoglobin content was 48% and the colour index 1. There were definite punctate basophilia and polychromasia and some nucleated red cells (normoblasts). It was noticed that the child could dorsiflex her wrist if the fingers were flexed, but not if the fingers were extended.

Cavity in the Lung.

Dr. McDonald's second patient was a child, aged three and a half years. The child had been admitted on September 15, 1928, for empyema on the left side. Subsequently she had had recurring attacks of bronchitis and three attacks of broncho-pneumonia. A large cavity was present. Dr. McDonald exhibited the skiagrams of her chest. He raised the question whether it would be better to treat the condition with avulsion of the phrenic nerve or to cause the chest wall to collapse on to the lung.

Osteomyelitis.

Dr. McDonald's third patient was a male, aged four years, who had been admitted on October 19, 1929, with a history of fever and illness of six days' duration. The child had had pain in the abdomen and vomiting for over a month. He had fallen and had hurt his back and neck prior to admission, but had appeared to be quite well at a later date. At the time of the meeting he had severe pain over and around the right posterior superior spine of the ilium. He had been unable to sit up; his legs and abdomen were stiff and rigid. He had less pain and the abdominal muscles were flaccid and lax. The pain was definitely localized over the sacro-iliac region. There was a swelling on the right side, low down in the back. No fluid had been found during an exploration with the needle. Dr. McDonald stated that the diagnosis lay between tetanus, anterior poliomyelitis and osteomyelitis. He was inclined to accept the last suggestion.

Thyreoglossal Cyst.

DR. G. P. DIXON presented a male child, aged seven years, who had a swelling in the neck over the thyreoid gland. The swelling had been noticed twenty-four hours previously. Ten days before admission the child had had a sore on the corner of the mouth and a swelling under the chin. Both had disappeared. There was a tense swelling not tender, over the thyreoid gland. It was beginning to decrease in size. Dr. Dixon considered that it was a thyreoglossal cyst.

Proceedings of the Australian Medical Boards.

VICTORIA.

THE undermentioned have been registered under the provisions of Part I of the *Medical Act*, 1928, of Victoria, as duly qualified medical practitioners:

Adamson, Charles Henry Bruce, M.B., Ch.B., 1927 (Univ. Edinburgh), 57, Wilson Street, Brighton, S.5.

Colquhoun, John Boyd, M.B., Ch.B., 1925 (Univ. Edinburgh), "Tasma," Parliament Place, East Melbourne.

Nelson (*née* Smith), Edna Lillian, M.B., Ch.M., 1902 (Univ. Sydney), North Road, Ormond.

Additional qualification registered:

Fitts, Clive Hamilton, M.D., 1929 (Melbourne).

Obituary.

FRANCIS JOHN DRAKE.

FRANCIS JOHN DRAKE, whose death was announced in our issue of January 4, 1930, was born in Melbourne in December, 1860. His father, the late John Drake, was a schoolmaster in Kew, Victoria. After he left school he entered the University of Melbourne. He first went through the Arts course and obtained the degree of Bachelor of Arts. Later he entered the medical school and distinguished himself in passing through the course without difficulty. Just before he completed his studies the curriculum was recast. He obtained his degrees in medicine and surgery in 1888. He also obtained the degree of Master of Arts. After graduation he served for twelve months as a resident medical officer at the Melbourne Hospital. It appears that during this period of service he manifested a preference for surgery. In 1890 he was appointed Surgeon-Superintendent at the Launceston General Hospital. The opportunities offered by the conditions attaching to this position for a man with aptitude for surgery are well known and it is small wonder that Francis John Drake acquired exceptional skill and dexterity as an operator during the eight years' service at Launceston. In addition he proved himself a highly competent diagnostician and a sound practitioner. He paid a visit to England before he resigned the position of Surgeon-Superintendent. In 1898 he commenced practice in Macquarie Street, Hobart, chiefly devoting himself to surgery. In 1903 he was compelled to relinquish his practice on account of ill health. As is pointed out by Dr. Edward Gault, his illness determined him to give up his career as a surgeon and to turn his attention to tuberculosis. In 1906 he founded a sanatorium for tuberculous patients at Mitcham, Victoria. He planned the institution with care and devoted much attention to the proper organization and conduct of the establishment. His undertaking was eminently successful. In 1913 he travelled to Europe and America and visited many of the well known sanatoria in England, Switzerland and America. He returned to Australia soon after the outbreak of war. He was at that time fifty-four years of age and was not in a physical condition to offer himself for service overseas. In March, 1918, he joined the Australian Army Medical Corps Reserve and was placed in charge of the sanatorium at Mont Park. He was given the rank of Major. Here, as at Mitcham, he did excellent work and his wide experience and sound judgement proved of great benefit to his patients. He continued to work at Mitcham until 1926, when the sanatorium was closed. In the meantime he practised as a consultant in Collins Street, Melbourne.

He was thorough in all he undertook and when he started his special work in tuberculosis, he devoted time and energy in original investigations. Of his personal qualities Dr. Gault is qualified to speak, for he enjoyed a long friendship with Francis John Drake. He has left a widow and a family. Dr. F. J. B. Drake, of Swansea, Tasmania, is one of his sons.

Dr. Edward L. Gault writes:

Adversity is the touchstone of character. It revealed the manly virtue of Frank Drake just at the moment when he had won the rank of Tasmania's leading surgeon. While still a young man and burdened by the responsibility of a young family, he was abruptly halted by the development of pulmonary tuberculosis. It was the day of sanatorium treatment and Drake with characteristic thoroughness set aside all his engagements and spent a year in an effort to recover health. He accepted a rule of absolute silence and for eighteen months communicated with his friends only by the signs of the deaf and dumb language.

Treatment was partially successful. His slight figure was transformed to Pickwickian proportions, but he was henceforth a crippled man. The arduous life he had lived was no longer possible. He had to forsake his chosen field of surgery and recast his programme of professional life. This he did in a radical fashion by opening what I believe was the first modern sanatorium for tuberculosis in Victoria at Mitcham. There he spent many years in sound work, being himself an example and an encouragement to his patients.

For the rest he was a true friend, a man of cheery optimism and the possessor of a gift of whimsical humour which made him tolerant of the follies and weaknesses of his fellows.

Books Received.

A SYSTEM OF BACTERIOLOGY IN RELATION TO MEDICINE: (Privy Council, Medical Research Council); Volume II; 1929. London: His Majesty's Stationery Office. Crown 4to., pp. 420. Price: one guinea.

THE CANCER PROCESS, by J. J. M. Shaw, M.A., M.D., F.R.C.S.E.; 1930. Edinburgh: E. and S. Livingstone. Royal 8vo., pp. 16. Price: 1s. net.

THE PRACTICAL MEDICINE SERIES: THE EYE, EAR, NOSE AND THROAT, Edited by C. P. Small, M.D., A. H. Andrews, M.D., and G. E. Shambaugh, M.D.; Series 1929. Chicago: The Year Book Publishers. Crown 8vo., pp. 574, with illustrations. Price: $2.50 net.

Diary for the Month.

Mar. 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Mar. 13.—Victorian Branch, B.M.A.: Council.
Mar. 13.—Surgical Section, Queensland Branch, B.M.A.
Mar. 14.—Queensland Branch, B.M.A.: Council.
Mar. 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Mar. 19.—Section of Obstetrics and Gynæcology, New South Wales Branch, B.M.A.
Mar. 19.—Eye, Ear, Nose and Throat Section, Queensland Branch, B.M.A.
Mar. 20.—New South Wales Branch, B.M.A.: Branch (annual).
Mar. 25.—New South Wales Branch, B.M.A.: Council.
Mar. 26.—Victorian Branch, B.M.A.: Council.
Mar. 27.—South Australian Branch, B.M.A.: Branch.
Mar. 28.—Federal Committee of B.M.A. in Australia.
Mar. 28.—Queensland Branch, B.M.A.: Council.

Medical Appointments.

Dr. E. J. Howley (B.M.A.) has been appointed Medical Superintendent of the Amherst District Hospital and Sanatorium, Talbot, and Medical Officer of Health to the Talbot Shire Council, Victoria.

* * *

Dr. Philip Cornelius Hogan has been appointed Resident Medical Officer at the Parkside Mental Hospital, South Australia.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xx.

Kynuna District Hospital, Queensland: Female Medical Officer.

Mater Misericordiæ General Hospital, North Sydney: Honorary Vacancies.

Saint Margaret's Hospital, Bourke Street, Sydney: Resident Medical Officer.

The Women's Hospital, Crown Street, Sydney: Honorary Assistant Anæsthetist.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
New South Wales: Honorary Secretary, 21, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phœnix Mutual Provident Society.
Victorian: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
Queensland: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting apopintments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Mount Isa Hospital.
South Australian: Secretary, 207, North Terrace, Adelaide.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia. Booleroo Centre Medical Club.
Western Australian: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
New Zealand (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales.

Editorial Notices.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary be stated.

All communications should be addressed to "The Editor," The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Subscription Rates.—Medical students and others not receiving The Medical Journal of Australia in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.